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* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

NEWS  1              Web Page URLs for STN Seminar Schedule - N. America
NEWS  2              "Ask CAS" for self-help around the clock
NEWS  3   JAN 27     Source of Registration (SR) information in REGISTRY updated
                     and searchable
NEWS  4   JAN 27     A new search aid, the Company Name Thesaurus, available in
                     CA/CAplus
NEWS  5   FEB 05     German (DE) application and patent publication number format
                     changes
NEWS  6   MAR 03     MEDLINE and LMEDLINE reloaded
NEWS  7   MAR 03     MEDLINE file segment of TOXCENTER reloaded
NEWS  8   MAR 03     FRANCEPAT now available on STN
NEWS  9   MAR 29     Pharmaceutical Substances (PS) now available on STN
NEWS 10   MAR 29     WPIFV now available on STN
NEWS 11   MAR 29     New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS 12   APR 26     PROMT: New display field available
NEWS 13   APR 26     IFIPAT/IFIUDB/IFICDB: New super search and display field
                     available
NEWS 14   APR 26     LITALERT now available on STN
NEWS 15   APR 27     NLDB: New search and display fields available
NEWS 16   May 10     PROUSDDR now available on STN
NEWS 17   May 19     PROUSDDR: One FREE connect hour, per account, in both May
                     and June 2004
NEWS 18   May 12     EXTEND option available in structure searching
NEWS 19   May 12     Polymer links for the POLYLINK command completed in REGISTRY
NEWS 20   May 17     FRFULL now available on STN
NEWS 21   May 27     STN User Update to be held June 7 and June 8 at the SLA 2004
                     Conference
NEWS 22   May 27     New UPM (Update Code Maximum) field for more efficient patent
                     SDIs in CAplus
NEWS 23   May 27     CAplus super roles and document types searchable in REGISTRY
NEWS 24   May 27     Explore APOLLIT with free connect time in June 2004

NEWS EXPRESS  MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
              MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
              AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
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NEWS LOGIN    Welcome Banner and News Items
NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
NEWS WWW      CAS World Wide Web Site (general information)

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21
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DICTIONARY FILE UPDATES:  14 JUN 2004  HIGHEST RN 693217-50-4

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COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                0.42       0.63

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FILE COVERS 1907 - 15 Jun 2004  VOL 140 ISS 25
FILE LAST UPDATED: 14 Jun 2004  (20040614/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> s mcp-1
          7065 MCP
           380 MCPS
          7225 MCP
                 (MCP OR MCPS)
       7920631 1
L1        3461 MCP-1
                 (MCP(W)1)
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=> s l1 and inflammat? () disease?
        179141 INFLAMMAT?
        781585 DISEASE?
          8111 INFLAMMAT? (W) DISEASE?
L2         110 L1 AND INFLAMMAT? (W) DISEASE?

=> s l2 and review/dt
       1734424 REVIEW/DT
L3           14 L2 AND REVIEW/DT

=> d l3, ibib abs, 1-14

L3   ANSWER 1 OF 14  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:         2004:214309  HCAPLUS
DOCUMENT NUMBER:          140:355356
TITLE:                    Cytokines and steroidogenesis
AUTHOR(S):                Bornstein, S. R.; Rutkowski, H.; Vrezas, I.
CORPORATE SOURCE:         Department of Endocrinology, University Hospital of
                          Duesseldorf, Duesseldorf, 40225, Germany
SOURCE:                   Molecular and Cellular Endocrinology (2004), 215(1-2),
                          135-141
                          CODEN: MCEND6; ISSN: 0303-7207
PUBLISHER:                Elsevier Science Ltd.
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB   A review.  Cytokines interfere with steroidogenesis at the level of the
     adrenals, testes, and ovaries.  Within the adrenal, macrophages, and
     lymphocytes, physiol. widely infiltrating the adrenal cortex, and
     adrenocortical, and chromaffin cells produce cytokines, as IL-1, IL-6,
     TNFα, leukemia inhibitory factor (LIF), and IL-18 which have a key
     role in the immune-adreno-cortical communication.  In addn. to cytokines
     interacting with adrenal function, cytokine independent mechanisms are
     responsible for a cell to cell-mediated immune regulation of the adrenal.
     The importance of this immune-endocrine cross-talk becomes evident in the
     case of autoimmune and inflammatory diseases being necessary for an
     adequate adrenal stress response.  Secretory products of macrophages are
     involved in the regulation of steroidogenesis, Sertoli cell activity, and
     germ cell survival in the human testes.  In rats, IL-1 is involved in the
     paracrine regulation of Leydig cell steroidogenesis.  IL-6 has been
     suggested to exert adverse effects on the male reproductive function,
     inducing persistent testicular resistance to LH action and/or suppression
     of Leydig cell steroidogenesis.  Cytokines such as IL-8 and MCP-1
     (monocyte chemotactic protein-1) are involved in follicular development
     and atresia, ovulation, steroidogenesis, and corpus luteum function.  In
     undifferentiated ovarian cells TNF and IL-1 inhibit steroidogenesis,
     whereas in differentiated ovaries these cytokines stimulate progesterone
     synthesis.  Some ovarian cancer cells secrete TNF and IL-1 which stimulate
     growth of these cells.  In conclusion, cytokines interact with
     steroidogenesis in a systemic and complex manner, influencing development,
     function, and hormone prodn. of the adrenals, testes, and ovaries.
REFERENCE COUNT:          41    THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS
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L3   ANSWER 2 OF 14  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:         2003:914646  HCAPLUS
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DOCUMENT NUMBER: 140:296596
TITLE: Anti **MCP-1** gene therapy effective for **inflammatory diseases**.
AUTHOR(S): Kitamoto, Shiro; Egashira, Kensuke
CORPORATE SOURCE: Graduate School of Medicine, Kyushu University, Japan
SOURCE: Bio Industry (2003), 20(10), 44-53
CODEN: BIINEG; ISSN: 0910-6545
PUBLISHER: Shi Emu Shi Shuppan
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese
AB A review. Monocyte chemoattractant protein-1 (**MCP-1**) mediated **inflammatory diseases** as well as anti **MCP-1** gene therapy with mutant **MCP-1** gene(7ND) as anti-inflammatory agent is reviewed with mechanism and examples.

L3 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2003:837629 HCAPLUS
DOCUMENT NUMBER: 139:349317
TITLE: Arteriosclerosis, restenosis, and inflammation
AUTHOR(S): Kitamoto, Shiro; Egashira, Kensuke
CORPORATE SOURCE: Grad. Sch. Med., Kyushu Univ., Japan
SOURCE: Kekkan Igaku (2003), 4(5), 481-489
CODEN: KIEGA2; ISSN: 1345-9031
PUBLISHER: Medikaru Rebyusha
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese
AB A review on (1) pathogenesis of atherosclerosis as a chronic **inflammatory disease**, (2) roles of **MCP-1** in atherogenesis, (3) inhibition of atherogenesis by a mutant **MCP-1** gene, (4) importance of inflammation in the pathogenesis of restenosis after angioplasty or stent implantation, (5) roles of **MCP-1** in restenosis, and (6) inhibition of restenotic changes (neointimal hyperplasia) after balloon injury by anti-**MCP-1** gene therapy in animals.

L3 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2003:521663 HCAPLUS
DOCUMENT NUMBER: 139:274519
TITLE: Chemokine Receptors in Vascular Smooth Muscle
AUTHOR(S): Schecter, Alison D.; Berman, Adriane B.; Taubman, Mark B.
CORPORATE SOURCE: The Zena and Michael A. Wiener Cardiovascular Institute, New York, NY, USA
SOURCE: Microcirculation (New York, NY, United States) (2003), 10(3/4), 265-272
CODEN: MROCER; ISSN: 1073-9688
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Atherosclerosis is considered to be an **inflammatory disease**. Chemokines are low-mol.-wt. proteins that exert their effects, in part, through mediating leukocytic infiltration into the vessel wall. Recently, studies have detd. that chemokines and their receptors are present, and function on other cellular components comprising the arterial wall, such as the endothelium and vascular smooth muscle. Smooth muscle cells (SMC) constitute the major cellular element of the arterial wall and are located predominantly in the arterial media. Recent studies have

demonstrated that SMC possess a no. of functional chemokine receptors, including CCR5, CXCR4, and a receptor for monocyte chemoattractant protein-1 (**MCP-1**). It is likely that SMC are increasingly recognized as potential targets for chemokines, and that these effects may influence a variety of normal and pathol. processes involving SMC such as atherosclerosis and arterial injury.

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:521661 HCAPLUS
DOCUMENT NUMBER: 139:275277
TITLE: Monocyte Chemoattractant Protein-1 (CCL2) in **Inflammatory Disease** and Adaptive Immunity: Therapeutic Opportunities and Controversies
AUTHOR(S): Daly, Christine; Rollins, Barrett J.
CORPORATE SOURCE: Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA, 02115, USA
SOURCE: Microcirculation (New York, NY, United States) (2003), 10(3/4), 247-257
CODEN: MROCER; ISSN: 1073-9688
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Monocyte chemoattractant protein (**MCP**)-**1** (CCL2) specifically attracts monocytes and memory T cells. Its expression occurs in a variety of diseases characterized by mononuclear cell infiltration, and there is substantial biol. and genetic evidence for its essential role in atherosclerosis and multiple sclerosis. Despite intensive screening, there are as yet no small-mol. antagonists of the receptor of **MCP-1**/CCL2, CCR2. However, biol. agents, including antibodies and inhibitory peptides, have been developed and may be useful for these indications. Recent evidence from genetically modified mice indicates that **MCP-1** and CCR2 have unanticipated effects on T helper (Th) cell development. However, unlike the identical phenotypes of **MCP-1**/CCL2-/- and CCR2-/- mice in **inflammatory diseases**, the phenotypes of these mice are disparate in adaptive immunity: **MCP-1** stimulates Th2 polarization, whereas CCR2 activation stimulates Th1 polarization. This presents both a challenge and an opportunity for targeting the **MCP-1**/CCL2/CCR2 axis in disease.

REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:147195 HCAPLUS
DOCUMENT NUMBER: 138:318367
TITLE: Inflammation and coronary artery disease
AUTHOR(S): Ikeda, Uichi
CORPORATE SOURCE: Division of Cardiovascular Medicine, Jichi Medical School, Tochigi, 329-0498, Japan
SOURCE: Current Vascular Pharmacology (2003), 1(1), 65-70
CODEN: CVPUAY; ISSN: 1570-1611
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Several evidences, ranging from in vitro expts., pathol. anal.

and epidemiol. studies, show that atherosclerosis is intrinsically an **inflammatory disease**. The plasma concns. of interleukin-6 (IL-6) and its hepatic byproduct, C-Reactive Protein (CRP), appear to reflect the intensity of occult plaque inflammation and by inference may det. the vulnerability of plaque rupture. The monocyte chemoattractant protein-1 (**MCP-1**) plays a crucial role in initiating coronary artery disease by recruiting monocytes/macrophages to the vessel wall. This leads to the formation of atherosclerotic lesions and also increases the vulnerability of the plaque. Indeed, circulating IL-6 and **MCP-1** levels are elevated in patients with acute myocardial infarction, and also in patients with unstable angina, but not in those with stable angina. The plasma IL-6 and **MCP-1** concns. are also increased after percutaneous coronary intervention (PCI), and late restenosis is correlated with an increase in IL-6 or **MCP-1** concns. after the procedure. This finding suggests that the expression of IL-6 and **MCP-1** may not only be related to the instability of atheromatous plaques, but also to the formation of restenotic lesions after PC1. The development of drugs specifically targeted against IL-6 and **MCP-1** may be useful in the prevention of plaque formation, myocardial infarction and restenosis.

REFERENCE COUNT: 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:340967 HCAPLUS
DOCUMENT NUMBER: 137:292993
TITLE: Chemokines in health and disease
AUTHOR(S): Gangur, Venu; Birmingham, Neil P.; Thanesvorakul, Sirinart
CORPORATE SOURCE: Department of Food Science and Human Nutrition, Food Allergy and Immunology Laboratory, Michigan State University, East Lansing, MI, 48824, USA
SOURCE: Veterinary Immunology and Immunopathology (2002), 86(3-4), 127-136
CODEN: VIIMDS; ISSN: 0165-2427
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Chemokines belong to a large family of structurally related proteins that play a pivotal role in immune system development and deployment. While a large no. of chemokines (~50) and their receptors (~20) have been identified from humans or mice, only a few are known in domestic veterinary species. Recent data implicate CXCL8 (old name, IL-8), CXCL10 (old name, IP-10) (both CXC chemokines) and CCL2 (old name, **MCP-1**) (a CC chemokine) in veterinary infections, **inflammatory diseases** or reprodn. There is compelling evidence for neutrophil targeting chemokines such as CXCL8, in ovine bacterial mastitis, bovine pneumonic pasteurellosis and equine chronic obstructive pulmonary disease (COPD). Monocyte and lymphocyte targeting chemokines appear to play a role in caprine arthritis encephalitis (CCL2) and canine endotoxemia (CXCL10). Interestingly CCL2 is considered a missing link between hormonal and cellular control of luteolysis. On the other hand, canine cardiovascular conditions are assocd. with overexpression of CCL2 and CXCL8. Furthermore, a no. of veterinary viral pathogens encode chemokine/chemokine receptor like mols. or chemokine binding proteins that may help viruses to evade the immune system. Here, we provide an overview of the chemokine system and critically evaluate the current literature implicating chemokines in veterinary pathophysiol. Furthermore, we highlight promising areas for further research and discuss how and why

chemokine antagonists are viewed as next generation anti-inflammatory drugs for the 21st century.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2001:506438 HCAPLUS
DOCUMENT NUMBER: 135:282560
TITLE: Inhibitors of monocyte chemoattractant protein-1/CC ligand 2 and its receptor CCR2
AUTHOR(S): Howard, O. M. Zack; Yoshimura, Teizo
CORPORATE SOURCE: Laboratory of Molecular Immunoregulation, Center for Cancer Research, National Cancer Institute-Frederick, Frederick, MD, 21702-1201, USA
SOURCE: Expert Opinion on Therapeutic Patents (2001), 11(7), 1147-1151
CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with refs. Chemoattractant cytokines (chemokines) have been shown to be pro-inflammatory and are thus likely targets for therapeutic intervention. An agent that interferes with directed migration of leukocytes to an inflammatory site is potentially a candidate anti-inflammatory drug. A specific chemokine, monocyte chemoattractant protein (**MCP**)-**1** or CC ligand 2 (CCL2), and its receptor, CC-chemokine receptor 2 (CCR2), have been implicated in both acute and chronic inflammatory and autoimmune diseases assocd. with infiltration of monocytes, macrophages, dendritic cells, NK cells, basophils and memory T-cells. Genetic modification of CCL2 and CCR2 in murine models has demonstrated the potential for antagonists to prevent atherogenic vascular disease and autoimmune **inflammatory diseases**. Modified CCL2 peptides, which still bind but no longer activate CCR2, demonstrated the therapeutic potential of CCL2 inhibitors in animal models of arthritis. Several classes of small mol. wt. CCL2 inhibitors have also been shown to inhibit chemotaxis in response to CCL2 in vitro and in animal models. However, more work is needed to establish the clin. efficacy of these CCL2 inhibitors.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2001:460904 HCAPLUS
DOCUMENT NUMBER: 136:133047
TITLE: FcεRI-mediated activation of transcription factors in antigen-presenting cells
AUTHOR(S): Kraft, Stefan; Bieber, Thomas
CORPORATE SOURCE: Department of Dermatology, Friedrich Wilhelms University, Bonn, D-53105, Germany
SOURCE: International Archives of Allergy and Immunology (2001), 125(1), 9-15
CODEN: IAAIEG; ISSN: 1018-2438
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Professional antigen-presenting cells (APC) such as monocytes

and dendritic cells (DC) bearing high-affinity IgE receptors (FcεRI) efficiently present IgE-bound antigens to T cells. FcεRI expression is upregulated on APC from atopic donors, esp. in inflamed tissues. These data suggest a pathophysiol. concept of an IgE-mediated delayed-type hypersensitivity reaction in atopy. However, FcεRI ligation also leads to the synthesis of proinflammatory cytokines and other mols. involved in inflammatory reactions. The investigation of transcription factors mediating these effects has only recently commenced. In general, members of the NF-κB family are known to regulate APC function and differentiation, with the RelB subunit being esp. important in DC generation. In addn., Ikaros and PU.1 have also been shown to be essential factors for DC differentiation, whereas Oct-2 is upregulated by differentiation towards macrophages. Recently, FcεRI has been demonstrated to induce NF-κB activation via IκB-α serine phosphorylation and degrdn. in monocytes and DC. Inhibitors of NF-κB activation can suppress FcεRI-induced TNF-α and **MCP-1** release. Interestingly, in human epidermal Langerhans' cells (LC), NF-κB activation can only be obsd. when large amts. of FcεRI are present. In addn., the compn. of NF-κB complexes differs between monocytes, monocyte-derived DC, and LC, suggesting a cell type-specific regulation. Moreover, the transcription factor NFAT is induced upon FcεRI ligation in human APC. The elucidation of transcription factors involved in FcεRI signaling in APC should contribute to the employment of new inhibition strategies for the treatment of atopic and other **inflammatory diseases**.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:161843 HCAPLUS
DOCUMENT NUMBER: 130:336528
TITLE: Human endothelium as a source of multifunctional cytokines: molecular regulation and possible role in human disease
AUTHOR(S): Krishnaswamy, Guha; Kelley, Jim; Yerra, Lakshminarayan; Smith, J. Kelly; Chi, David S.
CORPORATE SOURCE: Department of Internal Medicine, James H. Quillen College of Medicine, East Tennessee State University, Johnson City, TN, 37614-0622, USA
SOURCE: Journal of Interferon and Cytokine Research (1999), 19(2), 91-104
CODEN: JICRFJ; ISSN: 1079-9907
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 138 refs. Endothelial cells, by virtue of their capacity to express adhesion mols. and cytokines, are intricately involved in inflammatory processes. Endothelial cells have been shown to express interleukin-1 (IL-1), IL-5, IL-6, IL-8, IL-11, IL-15, several colony-stimulating factors (CSF), granulocyte-CSF (G-CSF), macrophage CSF (M-CSF) and granulocyte-macrophage CSF (GM-CSF), and the chemokines, monocyte chemotactic protein-1 (**MCP-1**), RANTES, and growth-related oncogene protein-α (GRO-α). IL-1 and tumor necrosis factor-α (TNF-α) produced by infiltrating inflammatory cells can induce endothelial cells to express several of these cytokines as well as adhesion mols. Induction of these cytokines in endothelial cells has

been demonstrated by such diverse processes as hypoxia and bacterial infection. Recent studies have demonstrated that adhesive interactions between endothelial cells and recruited inflammatory cells can also signal the secretion of inflammatory cytokines. This cross-talk between inflammatory cells and the endothelium may be crit. to the development of chronic inflammatory states. Endothelial-derived cytokines may be involved in hematopoiesis, cellular chemotaxis and recruitment, bone resorption, coagulation, and the acute-phase protein synthesis. As many of these processes are crit. to the maturation of an inflammatory and reparative state, it appears likely that endothelial-derived cytokines play a crucial role in several diseases, including atherosclerosis, graft rejection, asthma, vasculitis, and sepsis. Genetic and pharmacol. manipulation of endothelial-derived cytokines provides an addnl. approach to the management of chronic **inflammatory diseases**.

REFERENCE COUNT: 138 THERE ARE 138 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:440575 HCAPLUS
DOCUMENT NUMBER: 129:215276
TITLE: Will **MCP-1** and RANTES take center stage in **inflammatory diseases** including asthma?
AUTHOR(S): Conti, Pio; Barbacane, Renato C.; Di Gioacchino, Mario; Reale, Marcella
CORPORATE SOURCE: Division of Immunology, Department of Oncology and Neurosciences, University of Chieti School of Medicine, Chieti, 66100, Italy
SOURCE: Allergy and Asthma Proceedings (1998), 19(3), 121-123
CODEN: AAPRFV; ISSN: 1088-5412
PUBLISHER: OceanSide Publications, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 27 refs. RANTES and **MCP-1** are potent pro-inflammatory cytokines that can chemoattract mast cells in addn. to other inflammatory cells. Recent studies show that RANTES and **MCP-1** may increase the no. of mast cell migration in bronchial mucosa during asthma. Therefore, an inhibitory effect of RANTES and **MCP-1** could play a role in controlling the inflammatory response in asthma and other **inflammatory diseases**.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1996:373932 HCAPLUS
DOCUMENT NUMBER: 125:55576
TITLE: Monocyte chemoattractant protein 1: A potential regulator of monocyte recruitment in **inflammatory disease**
AUTHOR(S): Rollins, Barrett J.
CORPORATE SOURCE: Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Molecular Medicine Today (1996), 2(5), 198-204
CODEN: MMTOFK; ISSN: 1357-4310
PUBLISHER: Elsevier Trends Journals
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review, with 35 refs. The appearance of specific types of leukocytes in inflammatory infiltrates may be governed by cell-specific chemoattractants called chemokines. In particular, monocyte chemoattractant protein 1 (**MCP-1**) has been implicated in diseases characterized by monocyte-rich infiltrates, including atherosclerosis, rheumatoid arthritis and multiple sclerosis. While we are beginning to understand the structural determinants that govern the activities of **MCP-1** in vitro, we know much less about its physiol. functions in vivo and its pathogenetic role in disease. However, recent data from genetically modified mice have begun to place **MCP-1** in a central position in monocyte trafficking and activation.

L3 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1995:849123 HCAPLUS
DOCUMENT NUMBER: 123:253793
TITLE: Cytokine receptor and signal transduction (from **inflammatory diseases**)
AUTHOR(S): Mukaida, Naofumi
CORPORATE SOURCE: Cancer Res. Inst., Kanazawa Univ., Kanazawa, 920, Japan
SOURCE: Ensho to Men'eki (1995), 3(5), 505-12
CODEN: ENMEFA; ISSN: 0918-8371
PUBLISHER: Sentan Igakusha
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese

AB A review with 25 refs. on receptors of IL-1, IL-6, TNF and chemokines (IL-8, MIP-1α, MCAF/**MCP-1**). Specifically, the mechanism for the signal transduction through those receptors were discussed from the inflammation.

L3 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1993:252701 HCAPLUS
DOCUMENT NUMBER: 118:252701
TITLE: Pathophysiological roles of cytokines in rheumatoid arthritis
AUTHOR(S): Matsushima, Kouji
CORPORATE SOURCE: Cancer Res. Inst., Kanazawa Univ., Kanazawa, 920, Japan
SOURCE: Ensho (1993), 13(1), 9-15
CODEN: ENSHEE; ISSN: 0389-4290
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese

AB A review, with 27 refs. Rheumatoid arthritis (RA) is a chronic **inflammatory disease** of joint synovium. Several cytokines, including TNF alpha, IL 1, GM-CSF, IL 6, IL 8, MCAF/**MCP-1**, PDGF, and TGF beta have been detected in joint tissue as well as in synovial fluids from joint of RA. Possible roles of these cytokines in controlling pathophysiol. state of RA joints were extensively discussed.

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(FILE 'HOME' ENTERED AT 19:25:27 ON 15 JUN 2004)

FILE 'REGISTRY' ENTERED AT 19:25:35 ON 15 JUN 2004

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     FILE 'HCAPLUS' ENTERED AT 19:25:39 ON 15 JUN 2004
L1          3461 S MCP-1
L2           110 S L1 AND INFLAMMAT? () DISEASE?
L3            14 S L2 AND REVIEW/DT

=> s l1 and rheumatoid? () arthrit?
          22731 RHEUMATOID?
          33719 ARTHRIT?
          19637 RHEUMATOID? (W) ARTHRIT?
L4          117 L1 AND RHEUMATOID? (W) ARTHRIT?

=> s l4 and review/dt
        1734424 REVIEW/DT
L5           11 L4 AND REVIEW/DT

=> s l5 not l3
L6            9 L5 NOT L3

=> d l6, ibib abs, 1-9

L6   ANSWER 1 OF 9  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:         2003:897175  HCAPLUS
DOCUMENT NUMBER:          139:379469
TITLE:                    Synovitis in rheumatoid arthritis and chemokines
AUTHOR(S):                Nanki, Toshihiro
CORPORATE SOURCE:         Grad. Sch., Tokyo Med. Dent. Univ., Japan
SOURCE:                   Ensho to Men'eki (2003), 11(6), 760-769
                          CODEN: ENMEFA; ISSN: 0918-8371
PUBLISHER:                Sentan Igakusha
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 Japanese
AB   A review on (1) classification of chemokines and their receptors, (2)
     expression of chemokines (MCP-1/CCL2, MIP-1α/CCL3,
     groα/CXCL1, IL-8/CXCL8, fractalkine/CX3CL1, etc.) in synovia in
     rheumatoid arthritis (RA) and their pathol. functions, (3) chemokine
     receptors expressed in inflammatory cells (T cells, macrophage-like
     synoviocytes, etc.), and (4) treatment of RA with chemokine antagonists.

L6   ANSWER 2 OF 9  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:         2003:158533  HCAPLUS
DOCUMENT NUMBER:          138:367164
TITLE:                    IL-17
AUTHOR(S):                Hamuro, Junji
CORPORATE SOURCE:         Japan
SOURCE:                   Biotherapy (Tokyo, Japan) (2003), 17(1), 85-97
                          CODEN: BITPE9; ISSN: 0914-2223
PUBLISHER:                Gan to Kagaku Ryohosha
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 Japanese
AB   A review.  IL-17 is a potent proinflammatory cytokine produced mainly by
     activated memory CD4-T cells.  The family of IL-17, a new family of
     cytokines, is composed of six functionally related members, ie, IL-17 and
     IL-17B-F in humans and mice.  IL-17 exerts its biol. activity as a
     homodimer.  In contrast to the selected expression pattern of this gene,
     the IL-17 receptor is ubiquitously distributed among diverse tissues and
     cells.  IL-17 induces the secretion of IL-6, IL-8, PGE2, MCP-1 and
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G-CSF by fibroblasts, keratinocytes, epithelial and endothelial cells, and is also able to induce ICAM-1 expression, T cell proliferation, and growth and differentiation of CD34+ human progenitors into neutrophils. The involvement of IL-17 in the rejection of allogeneic grafts has been demonstrated. The potent inflammatory actions that have been identified for IL-17 and the emerging assocns. with major human diseases, such as **rheumatoid arthritis** and allergic asthma, suggest that the family of IL-17 may have significant roles in the pathophysiol. of inflammatory processes. IL-17 induces prodn. of metalloproteinases and nitric oxide, responsible for the aggravation of arthritis and joint destruction. IL-17 can recruit and activate neutrophils in the airways, mediated by IL-8 and MIP-2. In addn., IL-17 stimulates human bronchial epithelial cells to release the neutrophil-activating factor IL-6.

L6 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

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ACCESSION NUMBER: 2003:149671 HCAPLUS
DOCUMENT NUMBER: 138:285649
TITLE: Targeting monocyte chemoattractant protein-1 signalling in disease
AUTHOR(S): Dawson, Janet; Miltz, Wolfgang; Mir, Anis K.; Wiessner, Christoph
CORPORATE SOURCE: Neurodegeneration Unit, Arthritis and Bone Metabolism Research, Basel, CH-4002, Switz.
SOURCE: Expert Opinion on Therapeutic Targets (2003), 7(1), 35-48
CODEN: EOTTAO; ISSN: 1472-8222
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Monocyte chemoattractant protein-1 (**MCP-1**) has been implicated in many inflammatory and autoimmune diseases. The G-protein-coupled receptor CCR-2B is probably the most important **MCP-1** receptor in vivo, and loss of **MCP-1** effector function alone is sufficient to impair monocytic trafficking in inflammation models. **MCP-1** signaling appears to be a relevant target, esp. in **rheumatoid arthritis** (RA). In RA patients, **MCP-1** is produced by synovial cells and infiltrating monocytes, plasma **MCP-1** concns. correlate with swollen joint count, and elevated serum **MCP-1** concns. were found in juvenile RA in patients with active disease. Modulation of **MCP-1** signaling in exptl. RA showed beneficial effects on inflammation and joint destruction. With respect to chronic neuroinflammation, a crit. role for **MCP-1** has been established in animal models for multiple sclerosis. In acute neuroinflammation, exptl. evidence for a detrimental role of **MCP-1** in stroke and excitotoxic injury has been found. Several selective small mol. wt. CCR-2B antagonists and **MCP-1**-blocking antibodies have been described. The proof for the validity of targeting **MCP-1** signaling in disease, however, has yet to be established in clin. trials.

REFERENCE COUNT: 156 THERE ARE 156 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:853386 HCAPLUS
DOCUMENT NUMBER: 138:121156
TITLE: Cytokine directed therapy in scleroderma: rationale,

current status, and the future
AUTHOR(S): Simms, Robert W.; Korn, Joseph H.
CORPORATE SOURCE: Rheumatoll. Sect., Dep. Med., Boston Univ. Sch. Med., Boston, MA, USA
SOURCE: Current Opinion in Rheumatology (2002), 14(6), 717-722
CODEN: CORHES; ISSN: 1040-8711
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. The hallmark of scleroderma is cutaneous and visceral fibrosis characterized and by increased biosynthesis of multiple matrix proteins by interstitial fibroblasts. Studies over recent years have delineated pathways involved in promoting matrix synthesis and elucidated the mol. pathways of regulation. Central to the regulation of fibrosis are extracellular mediators, called cytokines, which are elaborated by a variety of cells, including those in the immune system, vascular cells, and fibroblasts themselves. The concept that inhibiting or promoting the action of these naturally occurring profibrotic or antifibrotic mols., resp., is a rationale therapeutic approach to treating scleroderma and other fibrotic diseases finds support in animal studies and anticytokine therapy conducted in relation to **rheumatoid arthritis** and other disorders. This review looks at cytokines known or thought to play a role in scleroderma and/or other fibrotic states and at potential therapy directed at these mediators. Potential targets for therapy include transforming growth factor β (TGF-β), connective tissue growth factor (CTGF), IL-4, IL-13, **MCP-1**, and endothelin, among others.
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:296376 HCAPLUS
DOCUMENT NUMBER: 135:91124
TITLE: Anti-TNFα therapy of **rheumatoid arthritis**: what have we learned?
AUTHOR(S): Feldmann, Marc; Maini, Ravinder N.
CORPORATE SOURCE: Kennedy Institute of Rheumatology Division, Imperial College School of Medicine, London, W6 8LH, UK
SOURCE: Annual Review of Immunology (2001), 19, 163-196
CODEN: ARIMDU; ISSN: 0732-0582
PUBLISHER: Annual Reviews Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with 160 refs. **Rheumatoid arthritis** (RA), a systemic disease, is characterized by a chronic inflammatory reaction in the synovium of joints and is assocd. with degeneration of cartilage and erosion of juxta-articular bone. Many pro-inflammatory cytokines including TNFα, chemokines, and growth factors are expressed in diseased joints. The rationale that TNFα played a central role in regulating these mols., and their pathophysiol. potential, was initially provided by the demonstration that anti-TNFα antibodies added to in vitro cultures of a representative population of cells derived from diseased joints inhibited the spontaneous prodn. of IL-1 and other pro-inflammatory cytokines. Systemic administration of anti-TNFα antibody or sTNFR fusion protein to mouse models of RA was shown to be anti-inflammatory and joint protective. Clin. investigations in which the activity of TNFα in RA patients was blocked with i.v. administered infliximab, a chimeric anti-TNFα monoclonal antibody (mAB), has

provided evidence that TNF regulates IL-6, IL-8, **MCP-1**, and VEGF prodn., recruitment of immune and inflammatory cells into joints, angiogenesis, and redn. of blood levels of matrix metalloproteinases-1 and -3. Randomized, placebo-controlled, multi-center clin. trials of human TNFα inhibitors have demonstrated their consistent and remarkable efficacy in controlling signs and symptoms, with a favorable safety profile, in approx. two thirds of patients for up to 2 yr, and their ability to retard joint damage. Infliximab (a mAB), and etanercept (a sTNF-R-Fc fusion protein) have been approved by regulatory authorities in the United States and Europe for treating RA, and they represent a significant new addn. to available therapeutic options.

REFERENCE COUNT: 160 THERE ARE 160 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:520441 HCAPLUS
DOCUMENT NUMBER: 132:48615
TITLE: **MCP-1** in human disease insights gained from animal models
AUTHOR(S): Boring, Landin; Charo, Israel F.; Rollins, Barrett J.
CORPORATE SOURCE: The Gladstone Institute of Cardiovascular Disease and the Cardiovascular, University of California, San Francisco, CA, USA
SOURCE: Chemokines in Disease (1999), 53-65. Editor(s): Hebert, Caroline A. Humana: Totowa, N. J.
CODEN: 67ZKA8
DOCUMENT TYPE: Conference; **General Review**
LANGUAGE: English

AB A review with 53 refs. Topics discussed include kidney disease, delayed-type hypersensitivity reactions, **rheumatoid arthritis**, autoimmune encephalomyelitis, granulomatous lung disease, effects of overexpression of **MCP-1**, effects of targeted disruption of **MCP-1** expression, and effects of disruption of CCR2.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:680262 HCAPLUS
DOCUMENT NUMBER: 130:195340
TITLE: Chemokines in **rheumatoid arthritis**
AUTHOR(S): Szekanecz, Zoltan; Strieter, Robert M.; Kunkel, Steven L.; Koch, Alisa E.
CORPORATE SOURCE: Department of Medicine, Section of Arthritis and Connective Tissue Diseases, Department of Medicine, Northwestern University Medical School, Chicago, IL, 60611, USA
SOURCE: Springer Seminars in Immunopathology (1998), 20(1-2), 115-132
CODEN: SSIMDV; ISSN: 0344-4325
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 76 refs. Topics discussed include C-X-C chemokines, interleukin-8, ENA-78, Groα and Groβ, CATP-III, CC-chemokines, MIP-1, **MCP-1**, RANTES, and chemokine receptors.

REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1994:653116 HCAPLUS
DOCUMENT NUMBER: 121:253116
TITLE: The immunopathology of chemotactic cytokines
AUTHOR(S): Strieter, Robert M.; Kunkel, Steven L.
CORPORATE SOURCE: Medical School, University of Michigan, Ann Arbor, MI, 48109-0602, USA
SOURCE: Advances in Experimental Medicine and Biology (1993), 351(Chemokines), 19-28
CODEN: AEMBAP; ISSN: 0065-2598
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with 20 refs. of the evidence demonstrating the expression of specific chemotactic cytokines in assocn. with human disease, like lung disease, the presence of interleukin-8 and **MCP-1** in **rheumatoid arthritis**, and interleukin-8 in ischemia/reperfusion injury.

L6 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1993:166804 HCAPLUS
DOCUMENT NUMBER: 118:166804
TITLE: Relationship of histamine-releasing factors to the human intercrine/chemokine group of cytokine-like molecules
AUTHOR(S): Kaplan, Allen P.; Kuna, Piotr; Reddigari, Sesha; Rucinski, Doreen; Baeza, Maria; Oppenheim, Joost J.; Schall, Thomas J.
CORPORATE SOURCE: Health Sci. Cent., SUNY, Stony Brook, NY, 11794, USA
SOURCE: International Archives of Allergy and Immunology (1992), 99(2-4), 311-15
CODEN: IAAIEG; ISSN: 1018-2438
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review, with 37 refs. Histamine-releasing factors have been characterized as a product of human mononuclear cells and platelets. MCAF/**MCP-1**, a monocyte-derived product is the most potent one described which acts rapidly (within 1 min) upon basophils of >90% of subjects tested. RANTES, a product of a subpopulation of CD4+ lymphocytes acts similarly but is ~50% as potent. CTAP III/NAP-2, by contrast, is a platelet derived HRF of low potency. It is, however, a plentiful protein and NAP-2, is derived from CTAP III by cleavage with elastase. All are members of the intercrine/chemokine group of cytokine-like mols. many of which are chemotactic factors and/or activate other cells. Interleukin 8 (NAP-1), another chemokine inhibits histamine release induced by all known forms of HRF. Interleukin 3 is a primer of basophils but at high concns. can itself induce histamine release from a subpopulation (mainly atopic) of subjects. These proteins are thought to be important mediators of protracted inflammation and histamine release seen in allergic late phase reactions and, perhaps in specific disorders such as chronic urticaria, atopic dermatitis, scleroderma, and **rheumatoid arthritis**.

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     (FILE 'HOME' ENTERED AT 19:25:27 ON 15 JUN 2004)

     FILE 'REGISTRY' ENTERED AT 19:25:35 ON 15 JUN 2004

     FILE 'HCAPLUS' ENTERED AT 19:25:39 ON 15 JUN 2004
L1          3461 S MCP-1
L2           110 S L1 AND INFLAMMAT? () DISEASE?
L3            14 S L2 AND REVIEW/DT
L4           117 S L1 AND RHEUMATOID? () ARTHRIT?
L5            11 S L4 AND REVIEW/DT
L6             9 S L5 NOT L3

=> s l1 and glomerular? () nephritide?
         25308 GLOMERULAR?
            41 NEPHRITIDE?
             1 GLOMERULAR? (W) NEPHRITIDE?
L7           0 L1 AND GLOMERULAR? (W) NEPHRITIDE?

=> s l1 and glomer?
         40064 GLOMER?
L8         237 L1 AND GLOMER?

=> s l8 and review/dt
       1734424 REVIEW/DT
L9           19 L8 AND REVIEW/DT

=> d l9, ibib abs, 1-19

L9   ANSWER 1 OF 19  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:        2003:539804  HCAPLUS
DOCUMENT NUMBER:         140:174116
TITLE:                   Effect of salicylate on the monocyte chemoattractant
                         protein-1 expression and intracellular reactive oxygen
                         species formation in human mesangial cells
AUTHOR(S):               Kim, Suhnggwon
CORPORATE SOURCE:        Department of Internal Medicine, Seoul National
                         University College of Medicine, Seoul, S. Korea
SOURCE:                  Taehan Sinjang Hakhoechi (2003), 22(3), 257-260
                         CODEN: TSHACY; ISSN: 1225-0015
PUBLISHER:               Korean Society of Nephrology
DOCUMENT TYPE:           Journal; General Review
LANGUAGE:                Korean
AB   A review.  Salicylate inhibits activation of NF-κB, thereby inhibit
     the expression of MCP-1 and also inhibits lysophosphatidylchoine-
     caused ROS prodn.  Effects of nonsteroidal anti-inflammatory agents,
     including aspirin, on glomerulonephritis are discussed.

L9   ANSWER 2 OF 19  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:        2003:521662  HCAPLUS
DOCUMENT NUMBER:         139:275278
TITLE:                   Chemokine Receptor 2 (CCR2) in Atherosclerosis,
                         Infectious Diseases, and Regulation of T-Cell
                         Polarization
AUTHOR(S):               Charo, Israel F.; Peters, Wendy
CORPORATE SOURCE:        Gladstone Institute of Cardiovascular Disease, San
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Francisco, CA, 94141, USA
SOURCE: Microcirculation (New York, NY, United States) (2003), 10(3/4), 259-264
CODEN: MROCER; ISSN: 1073-9688
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Infiltration of tissues by monocyte-derived macrophages is a prominent component of a wide-range of diseases, including atherosclerosis, **glomerulonephritis**, encephalitis, infectious diseases, and virtually all syndromes characterized by chronic inflammation. The mol. signals responsible for this directed migration are incompletely understood, but members of the chemokine family, esp. the monocyte chemoattractant proteins (MCPs) (**MCP-1** to MCP-5) are emerging as key players. Cells that respond to the MCPs do so because they express chemokine receptor 2 (CCR2), the cognate receptor. This review will summarize evidence supporting a key role for CCR2 in the pathogenesis of atherosclerosis, infections with intracellular pathogens, and regulation of the type I adaptive immune response.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2002:937217 HCAPLUS
DOCUMENT NUMBER: 139:227602
TITLE: Monocyte chemoattractant protein-1 (**MCP-1**) in the kidney: does it more than simply attract monocytes?
AUTHOR(S): Viedt, Christiane; Orth, Stephan R.
CORPORATE SOURCE: Division of Cardiology, Department of Internal Medicine, Ruperto Carola University, Heidelberg, Germany
SOURCE: Nephrology, Dialysis, Transplantation (2002), 17(12), 2043-2047
CODEN: NDTREA; ISSN: 0931-0509
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review presents evidence supporting the role of monocyte chemoattractant protein-1 (**MCP-1**) in renal inflammation. The **MCP-1** mediated activation of tubular epithelial cells is consistent with the notion that **MCP-1** contributes to tubulointerstitial inflammation, which is a hallmark of progressive renal disease. The tubulointerstitial rather than **glomerular** damage correlates best with the loss of renal function and the risk of progression to end-stage renal failure. Recent data suggest that **MCP-1** is more than just a chemoattractant but rather can directly elicit an inflammatory response by inducing cytokine and adhesion mol. expression in the kidney.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2002:490338 HCAPLUS
DOCUMENT NUMBER: 137:276622
TITLE: Pathophysiological and clinical implications of AT1 and AT2 angiotensin II receptors in metabolic disorders: hypercholesterolaemia and diabetes

AUTHOR(S): Strawn, William B.
CORPORATE SOURCE: Centre d'Etudes de l'Hypertension et des Maladies Cardiovasculaires, Ecole de Medecine de l'Universite de Wake Forest, Etats-Unis, N. Z.
SOURCE: Drugs (2002), 62(Spec. Issue), 31-41
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: French
AB A review. The coexistence of hypercholesterolemia and diabetes dramatically and synergistically increases the risk of microvascular and macrovascular complications in patients. A single unifying mechanism of increased prodn. of reactive oxygen species (ROS) by angiotensin II (Ang II) may serve as a causal link between hyperglycemia and hypercholesterolemia and many of the major pathways responsible for atherogenic and diabetic disorders. Several lines of evidence suggest a crucial role for Ang II-mediated oxidative stress in the pathogenesis of hyperglycemia- and hypercholesterolemia-assocd. endothelial dysfunction. Endothelial dysfunction in these scenarios may be due to impaired nitric oxide (NO) synthesis and/or inactivation of endothelium-derived NO by ROS. That Ang II plays an important role in the development of atherosclerosis and **glomerulosclerosis** is supported by numerous studies indicating that angiotensin receptor blockers (ARBs) retard the progression of these diseases in both exptl. animal models and humans. Evidence indicates that Ang II contributes to atherogenesis at both transcriptional and translational levels by upregulating adhesion mol. mRNA and protein synthesis. The recent demonstration of Ang II AT2 receptors in the adult kidney and their potential to oppose the vasoconstrictive, antinatriuretic, and profibrotic properties of AT1 receptors suggests that the balance of intrarenal AT1 and AT2 receptors may be important in detg. the cellular responses to Ang II in diabetic nephropathy. Results of these studies suggest that hypercholesterolemia and hyperglycemia can induce a pro-inflammatory response within coronary arteries and the kidney **glomerulus**. This response involves prodn. of well described macrophage chemotactic and adhesion mols., which results in macrophage recruitment and the development of acute and chronic injury. **Glomerular** macrophage recruitment in exptl. diabetes occurs via Ang II-stimulated monocyte chemoattractant protein (**MCP**)-**1** expression, suggesting that the renin-angiotensin system is an important regulator of local **MCP-1** expression, and strongly implicating macrophage recruitment and activation in the pathogenesis of early diabetic **glomerular** injury. Diabetes-assocd. vascular complications may also involve an activation of the nuclear factor (NF)-.vkappa.B by hyperglycemia. NF-.vkappa.B activation is related to AT1 receptor-mediated pathways, and is believed to be dependent on activation of the Rho proteins belonging to the superfamily of low mol. wt. guanosine triphosphatases (GTPases) that regulate intracellular signaling. Preincubation of vascular smooth muscle cells with insulin doubled NF-.vkappa.B transactivation stimulated by Ang II and hyperglycemia, suggesting a potential mechanism for cross-talk between the renin-angiotensin system and hyperglycemia. Taken together, these data suggest that activation of the renin-angiotensin system is a mechanism for the initiation and progression of inflammatory cell infiltration found in early changes common to both hypercholesterolemia and hyperglycemia. While the base of information regarding ARBs in high-risk patients with diabetes and hypercholesterolemia is lacking, preclin. and pilot trial data suggest that the ARBs are reno- and vasculoprotective in these patients. Therapeutic blockade of Ang II AT1 receptors in diabetic and hypercholesterolemic humans by ARBs, with concomitant elevation in plasma and tissue Ang II levels, may provide vascular and renal protection not only by reducing AT1 receptor-mediated

pro-oxidative effects, but also by unopposed AT2 receptor stimulation.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 2001:613989 HCAPLUS
DOCUMENT NUMBER: 136:99960
TITLE: The role of tubular cells in the progression of renal damage: guilty of innocent?
AUTHOR(S): Schena, F. P.; Grandaliano, G.; Gesualdo, L.
CORPORATE SOURCE: Division of Nephrology, Department of Emergency and Organ Transplantation, University of Bari, Bari, 70124, Italy
SOURCE: Renal Failure (2001), 23(3 & 4), 589-596
CODEN: REFAE8; ISSN: 0886-022X
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review on the role of proximal tubular cells in the progression of renal damage using in vitro and in vivo studies performed in animal models and in humans. Renal damage is characterized by a decreased nephron mass, **glomerular** hyperfiltration and proteinuria, which permanently stimulates tubular cells in the prodn. of cytokines, growth factors and chemokines. These inflammatory mediators contribute to the progression of renal damage. Various studies on the mRNA expression of epidermal growth factor and monocyte-chemoattractant protein-1 (**MCP-1**) in renal biopsy in patients with renal disease demonstrated that the urinary concn. correlated with their expression at the renal level and that the urinary EGF/**MCP-1** ratio was a valuable marker for the monitoring of renal damage during and after therapy. These results suggest that the mol. biol. applied to renal biopsy may help in searching for urinary markers useful to monitor the progression of renal damage in patients with chronic nephropathies.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 2001:256060 HCAPLUS
DOCUMENT NUMBER: 134:250316
TITLE: Pathogenesis of diabetic nephropathy
AUTHOR(S): Kimura, Hideki
CORPORATE SOURCE: Dep. Clin. Lab. Med. Nephrol., Fac. Med., Fukui Med. Univ., 23-3 Shimoaizuki, Matsuoka, Fukui, 910-1193, Japan
SOURCE: Seibutsu Shiryo Bunseki (2000), 23(5), 393-400
CODEN: SSBUEL; ISSN: 0913-3763
PUBLISHER: Seibutsu Shiryo Bunseki Kagakkai
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese
AB A review with 44 refs. Diabetic nephropathy is well known to be a major cause of end-stage renal disease requiring dialysis treatment. Its pathol. features are characterized mainly by basement membrane thickening and extracellular matrix (ECM) accumulation. Recently gathering data from clin. and exptl. studies have revealed that hyperglycemia and genetic factors takes a pivotal role in pathogenesis of diabetic nephropathy. Hyperglycemia induces the following four pathol. conditions: **glomerular**

hyperfiltration or hypertension, mesangial cell dysfunction, glycation, and increased oxidative stress. **Glomerular** hyperfiltration may increase the expression of TGF-β and ICAM-1 via enhanced shear stress. Protein kinase C (PKC) activation arising from hyperglycemia causes mesangial cell dysfunction, leading to **glomerulosclerosis**. Advanced glycation endoproducts (AGE) may activate mesangial cell and macrophage via the receptors and glycated ECM may result in retarding its turnover. Hyperoxidative status due to increased PKC activity and AGE appear to induce the expression of redox-sensitive genes such as VEGF and **MCP-1**. These advancement in deciphering diabetic nephropathy may provide a useful clue to designing a novel therapeutic approach.

L9 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

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ACCESSION NUMBER: 2001:51694 HCAPLUS
DOCUMENT NUMBER: 135:3621
TITLE: How renal cytokines and growth factors contribute to renal disease progression
AUTHOR(S): Benigni, Ariela; Remuzzi, Giuseppe
CORPORATE SOURCE: Mario Negri Institute for Pharmacological Research, Bergamo, 24125, Italy
SOURCE: American Journal of Kidney Diseases (2001), 37(1, Suppl. 2), S21-S24
CODEN: AJKDDP; ISSN: 0272-6386
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 20 refs. Terminal renal failure is the final common fate of chronic nephropathies regardless of the type of original insult. After removal of a crit. no. of nephrons, adaptive hemodynamic changes in the remaining nephrons ensure enough filtration power to the kidney but are ultimately detrimental. Such changes are largely mediated by the local formation of angiotensin II (AII) and prevented by the use of angiotensin-converting enzyme inhibitors, which also limit the forced opening of large unselective pores in the **glomerular** barrier, restoring size selectivity. Recent studies suggested that proteins filtered through the **glomerular** capillary, previously considered a marker of the severity of renal lesions, might have intrinsic toxicity on the proximal tubular cells and a contributory role in the progression of renal damage. Protein overload of proximal tubular cells induced the secretion of endothelin-1 (ET-1), monocyte chemoattractant protein-1 (**MCP-1**), and regulated on activation, normal T expressed and secreted (RANTES) that was mainly directed toward the basolateral compartment of the cell. Evidence available in rat models of proteinuric renal disease shows that expression of genes encoding such vasoactive and proinflammatory mols. as ET-1, **MCP-1**, and RANTES was consistently upregulated, and synthesis of the corresponding peptides was enhanced in renal tissue. Addnl. mechanisms of proximal tubular cell activation leading to interstitial inflammation and matrix deposition are the filtration of protein-bound metals and hormones and deposition and activation of filtered complement. Limiting protein traffic and the biol. effect of excessive tubular protein reabsorption by drugs interfering with AII synthesis or biol. activity prevents renal disease progression.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:675454 HCAPLUS
DOCUMENT NUMBER: 132:178640
TITLE: **Glomerular** ultrafiltration and apical tubular action of IGF-I, TGF-β, and HGF in nephrotic syndrome
AUTHOR(S): Wang, Shi-Nong; LaPage, Janine; Hirschberg, Raimund
CORPORATE SOURCE: Division of Nephrology and Hypertension, Harbor-UCLA Medical Center and UCLA, Torrance, CA, USA
SOURCE: Kidney International (1999), 56(4), 1247-1251
CODEN: KDYIA5; ISSN: 0085-2538
PUBLISHER: Blackwell Science, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review, with 18 refs. In nephrotic **glomerulopathies**, there is ultrafiltration of high mol. wt. forms of insulin-like growth factor-I (IGF-I), hepatocyte growth factor (HGF), and transforming growth factor-β (TGF-β), which are bioactive in tubular fluid and act through apical tubular receptors. Exptl. evidence indicates that ultrafiltered IGF-I, HGF, and TGF-β may contribute to increased tubular phosphate and sodium absorption, synthesis of extracellular matrix proteins, and secretion of chemokines such as monocyte chemoattractant protein-1 (**MCP-1**). Through these mechanisms, **glomerular** proteinuria may contribute to tubulointerstitial pathobiol. in nephrotic syndrome.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:55502 HCAPLUS
DOCUMENT NUMBER: 130:250265
TITLE: Angiotensin II is involved in the progression of renal disease: importance of non-hemodynamic mechanisms
AUTHOR(S): Wolf, G.
CORPORATE SOURCE: Department of medicine, division of nephrology and osteology, University of Hamburg, Germany
SOURCE: Nephrologie (1998), 19(7), 451-456
CODEN: NEPHDY; ISSN: 0250-4960
PUBLISHER: Medecine et Hygiene
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review, with 51 refs. Several recent studies have provided clear evidence that angiotensin-converting enzyme (ACE)-inhibitors slow the progression of renal disease. These effects are mainly independent from a comitant redn. in systemic blood pressure. Thus, angiotensin II (Ang II) exerts other effects on the kidney which are involved in the loss of renal function. Ang II induces proliferation of cultured mesangial and **glomerular** endothelial cells. Our group was the first to demonstrate that Ang II stimulates hypertrophy of cultured proximal tubular cells. Ang II stimulates bioactivation and expression of transforming growth factor-β (TGF-β) in tubular MCT cells. This Ang II-mediated expression of TGF-β is due to an increase in transcriptional activity. A neutralizing anti-TGF-β antibody attenuates the Ang II-induced increase in protein synthesis in MCT cells suggesting that the hypertrophy is mediated by synthesis and activation of endogenous TGF-β. Proximal tubular cells undergoing Ang II-mediated hypertrophy are arrested in the G1-phase of the cell cycle and express typical G1-phase-assocd. genes. Induction of such G1-phase-assocd. early growth response genes have been also described in vivo after infusion of Ang II into the renal artery. This G1-phase arrest depends on the induction of

the cyclin-dependent kinase (CdK) inhibitor p27Kip1. P27Kip1 expression is stimulated after incubation of LLC-PK1 cells with Ang II or TGF-β and binds to cyclin D1-CdK4 complexes, inhibits their kinase activity, and hampers G1-phase exit. Ang II stimulates transcription of collagen type IV in MCT cells. In addn. to the classical a1 (IV) chain, a3 (IV) collagen, which has normally a restricted localization in the kidney, is also induced. This stimulation is mediated by endogenous synthesis and autocrine action of TGF-β because a neutralizing anti-TGF-β antibody as well as TGF-β antisense oligonucleotides attenuate Ang II-induced collagen type IV transcription and synthesis. In addn., Ang II exerts immunomodulatory effects on the kidney through the induction of chemokines such as **MCP-1** and RANTES. In conclusion, Ang II has emerged as a multifunctional acting as a growth factor and a profibrogenic cytokine, and even having inflammatory properties.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:202838 HCAPLUS
DOCUMENT NUMBER: 128:242707
TITLE: Chemokine. A target to renal diseases
AUTHOR(S): Wada, Takashi; Yokoyama, Hitoshi; Furuichi, Kengo; Kobayashi, Kenichi
CORPORATE SOURCE: Sch. Med., Kanazawa Univ., Kanazawa, 920, Japan
SOURCE: Saishin Igaku (1998), 53(4), 874-881
CODEN: SAIGAK; ISSN: 0370-8241
PUBLISHER: Saishin Igakusha
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese

AB A review with 15 refs., on pathophysiol. roles of chemokines, IL-8, and MCAF/**MCP-1**, in renal diseases and intervention of **glomerulonephritis** by antibodies to chemokines. Possible chemokine-targeted anti-inflammation therapy is also discussed.

L9 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:36193 HCAPLUS
DOCUMENT NUMBER: 128:126759
TITLE: Role of chemokines in nephritis
AUTHOR(S): Yokoyama, Hitoshi; Wada, Takashi
CORPORATE SOURCE: Sch. Med., Kanazawa Univ., Kanazawa, 920, Japan
SOURCE: Ensho to Men'eki (1997), Volume Date 1998, 6(1), 102-108
CODEN: ENMEFA; ISSN: 0918-8371
PUBLISHER: Sentan Igakusha
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese

AB A review with 10 refs. Human chemokine family members and their biol. activities, and expression of chemokine receptors and ligands are summarized. Monocyte chemotactic and activating factor (MCAF/**MCP-1**) participates in nephritis advancement by induction of monocytes/macrophages in many nephritis models including **glomerular** basement membrane (GBM) type nephritis. Participation of interleukin 8 (IL-8) and MCAF/**MCP-1** has been demonstrated in human nephritis. Anti-chemokine antibody exhibits therapeutic effects in immune complex type acute nephritis model, anti-GBM type nephritis model and Thy1.1 antibody nephritis model.

L9 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:567258 HCAPLUS
DOCUMENT NUMBER: 127:246188
TITLE: Effect of low-density lipoproteins on mesangial cell expression of monocyte chemoattractant peptides
AUTHOR(S): Kamanna, Vaijinath S.; Kirschenbaum, Michael A.
CORPORATE SOURCE: Nephrology Section, Department of Veterans Affairs Medical Center, Long Beach, CA, USA
SOURCE: Contributions to Nephrology (1997), 120(Lipids and the Kidney), 176-190
CODEN: CNEPDD; ISSN: 0302-5144
PUBLISHER: Karger
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with 65 refs. discussing monocyte chemoattractant peptides, chemoattractant peptides and renal disease, atherogenic lipoproteins and chemoattractant peptides, atherogenic lipoproteins and mesangial M-CSF and **MCP-1**, cholesterol synthesis and mesangial **MCP-1**, and pathobiol. inter-relationships among lipoproteins. monocytes, mesangial cells and chemoattractant peptides.
REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:279326 HCAPLUS
DOCUMENT NUMBER: 126:342120
TITLE: Chemokines and anti-chemokine therapy in renal diseases
AUTHOR(S): Yokoyama, Hitoshi
CORPORATE SOURCE: Igakubu, Kanazawa Daigaku, Kanazawa, 920, Japan
SOURCE: Nippon Naika Gakkai Zasshi (1997), 86(4), 689-694
CODEN: NNGAAS; ISSN: 0021-5384
PUBLISHER: Nippon Naika Gakkai
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese
AB A review with 10 refs. on interleukin-8 (IL-8) and monocyte chemotactic and activating factor (MCAF/**MCP-1**) and their biol. activities, chemokines in relation to exptl. nephritis, roles of chemokines in human renal diseases, and effects of anti-chemokine therapy.

L9 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:250454 HCAPLUS
DOCUMENT NUMBER: 126:304685
TITLE: Role of monocyte chemoattractant protein-1 (**MCP-1**) in **glomerulonephritis**
AUTHOR(S): Natori, Yasuhiro
CORPORATE SOURCE: Res. Inst., Int. Med. Cent. Japan, Tokyo, 162, Japan
SOURCE: Yakugaku Kenkyu no Shinpo (1997), Volume Date 1996, 13, 49-59
CODEN: YAKSEY; ISSN: 0914-4544
PUBLISHER: Yakugaku Kenkyu Shorei Zaidan
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese

AB A review with 18 refs. Recent studies suggest that monocytes/macrophages (M.vphi.) play an important role in the pathogenesis of various types of **glomerulonephritis**. Chemokines are a family of structurally related, low mol. wt. proteins that regulate leukocyte migration and CC chemokines are chemotactic mainly for M.vphi.. The authors discuss the expression of CC chemokines in 2 exptl. models of **glomerular** disease in which M.vphi. are shown to be essential for the progression of the disease. The induction of these chemokines in kidneys of the 2 models corresponded with M.vphi. infiltration. The results suggest that members of CC chemokines play similar but distinct roles in the recruitment and activation of leukocytes in renal diseases and that the induction pattern of the gene expression of chemokines is not identical in renal diseases, and depends on the sites, grades, and/or types of injury in the kidney. Treatment with glucocorticoid ameliorated M.vphi. infiltration, crescent formation, and reduced urinary protein excretion. Since glucocorticoid inhibited the prodn. of chemokines in the model in vivo and also in cultured **glomerular** cells, the prodn. of chemokines might be one of the target sites of glucocorticoid.

L9 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:208454 HCAPLUS
DOCUMENT NUMBER: 126:275575
TITLE: Cell surface molecules and renal diseases
AUTHOR(S): Kawasaki, Katsutoshi; Fujinaka, Hidehiko; Yaoita, Eishin; Yamamoto, Tadashi; Kihara, Itaru
CORPORATE SOURCE: Dep. Pathology, Niigata Univ. Sch. Med., Niigata, 951, Japan
SOURCE: Ensho (1997), 17(1), 23-32
CODEN: ENSHEE; ISSN: 0389-4290
PUBLISHER: Nippon Ensho Gakkai Jimukyoku
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese

AB A review with 33 refs., on class and characteristics of Masugi nephritis, role of adhesion mols., expression of adhesion mol. in kidney and in pathol. situation, etc. Masugi nephritis of WKY rats, that is characterized with the early infiltration of CD8 pos. lymphocytes and monocytes/macrophages, developed severe proliferative **glomerulonephritis** with crescent formation. In this model, the expression of ICAM-1 and the infiltration of LFA-1 pos. cells were increased in the **glomeruli**. Th blocking studies of CD8, ICAM-1, LFA-1 and **MCP-1** in this model were effective for protection of proteinuria and **glomerular** injury. From these data, cell surface mols. such as adhesion mols. may play important roles in the **glomerulonephritis**.

L9 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1996:503490 HCAPLUS
DOCUMENT NUMBER: 125:165170
TITLE: Use of blocking antibodies as probes for in vivo functions of chemokines
AUTHOR(S): Harada, Akihisa; Mukaida, Naofumi; Matsushima, Kouji
CORPORATE SOURCE: Dep. Pharmacol., Kanazawa Univ., Kanazawa, 920, Japan
SOURCE: Methods (San Diego) (1996), 10(1), 166-174
CODEN: MTHDE9; ISSN: 1046-2023
PUBLISHER: Academic
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 84 refs. Leukocyte infiltration into an inflammatory site is one of the pathol. hallmarks of inflammatory reaction. Locally produced chemotactic factors are presumed to mediate the sequence of events leading to tissue injury assocd. with the infiltration of leukocytes. Chemotactic cytokines (chemokines) have been identified as being produced by various types of cells upon stimulation with inflammatory stimuli and exhibit a variety of effects on leukocytes in vitro and in vivo. Administration of highly specific neutralizing antibodies against these chemokines in several types of animal inflammation models clearly suggests important roles of these chemokines in recruiting and activating specific types of leukocytes at the inflammatory sites. Anti-IL-8 Ab treatment prevented neutrophil-dependent tissue damage as well as neutrophil infiltration in lipopolysaccharide (LPS)-induced dermatitis, LPS/IL-1-induced arthritis, lung reperfusion injury, and acute immune complex type **glomerulonephritis** in rabbits. Moreover, anti-**MCP-1** Ab and anti-RANTES Ab inhibited macrophage infiltration in IgA immune complex alveolitis in rats and influx of lung macrophages in a murine model of endotoxemia, resp. The use of anti-MIP-1α Ab also revealed that MIP-1α mediates eosinophil infiltration in allergic, granulomatous reactions in vivo.

L9 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1996:398409 HCAPLUS
DOCUMENT NUMBER: 125:54910
TITLE: Experimental **glomerulosclerosis**: Defektheilung of the kidney
AUTHOR(S): Schiller, Brigitte; Moran, John
CORPORATE SOURCE: Evanston Hospital, Northwestern University, Evanston, IL, USA
SOURCE: Artificial Organs (1996), 20(5), 445-450
CODEN: ARORD7; ISSN: 0160-564X
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 50 refs. Research in the role of cytokines in exptl. **glomerulonephritis** has increased our understanding of the mechanisms that may be involved in the development of progressive renal disease. **Glomerulosclerosis**, the final common pathway in a variety of underlying kidney diseases, is characterized by increased extracellular matrix formation and cell proliferation. Transforming growth factor-β (TGF-β) and monocyte chemoattractant protein-1 (**MCP-1**) have been identified in animal models as mediators in the processes that follow renal injury. There is evidence of similar events occurring in other fibrotic disorders, suggesting that there is a common generic pathway of fibrosis. This review summarizes the authors knowledge of TGF-β and **MCP-1** in exptl. kidney disease and compares these results with mechanisms described in other organs. The authors propose that **glomerulosclerosis** represents Defektheilung (healing by secondary intention) of the kidney after various injuries. The growing knowledge of the mechanisms involved will help advance future therapeutic interventions by directing the healing process toward primary healing.

L9 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1996:387965 HCAPLUS
DOCUMENT NUMBER: 125:139894

TITLE: IgA nephropathy. Overview
AUTHOR(S): Endoh, Masayuki; Sakai, Hideto
CORPORATE SOURCE: Sch. Med., Tokai Univ., Isehara, 259-11, Japan
SOURCE: Igaku no Ayumi (1996), 177(8), 521-524
CODEN: IGAYAY; ISSN: 0039-2359
PUBLISHER: Ishiyaku
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese

AB A review with 22 refs. The mechanism of the onset of IgA nephropathy is discussed for anti-Haemophilus parainfluenzae antibody, anomaly in hinge-region carbohydrate chain, and elevated prodn. of active oxygen species through Fcα receptor. Macrophage plays an important role in progression of IgA nephropathy though chemoattractant of monocyte chemoattractant protein-1 (**MCP-1**) and induction of inducible NO synthetase. Natural killer (NK) cells produced interferon γ in the nephropathy. The expression of thromboxane synthetase (TXS) is elevated, and arachidonic acid metabolites participates in global sclerosis and collapse in obsolescence in **glomerulus**. Therapy of IgA nephropathy is discussed including the effects of steroids and fish oil.

L9 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1995:967893 HCAPLUS
DOCUMENT NUMBER: 124:5906
TITLE: Role of atherogenic lipoproteins in cytokine-mediated renovascular injury
AUTHOR(S): Kirschenbaum, Michael A.; Pai, Rama; Roh, Daeyoung D.; Kamanna, Vaijinath S.
CORPORATE SOURCE: Dep . Veteran Affairs Med. Cent., Univ. California, Irvine, CA, USA
SOURCE: Mineral and Electrolyte Metabolism (1995), Volume Date 1996, 22(1-3), 47-50
CODEN: MELMDI; ISSN: 0378-0392
PUBLISHER: Karger
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 20 refs. Recent advances have clarified many basic cellular and mol. mechanisms assocd. with **glomerular** injury. The authors propose that atherogenic lipoproteins (e.g., native LDL and it more atherogenic oxidized variants) play a central role as biol. modifiers in monocyte- and cytoregulatory peptide-induced **glomerulosclerosis**. Following lipoprotein activation of mesangial and other intrinsic **glomerular** cells, monocytes adhere, transmigrate, differentiate, and proliferate within the **glomerular** mesangium. These events are mediated by increased expression of adhesion mols. (ICAM-1, VCAM-1, etc.) and specific monocyte chemoattractants (M-CSF, **MCP-1**, etc.). Furthermore, atherogenic lipoprotein can activate mesangial cells to express addnl. proinflammatory cytokines (TNF-α, TGF-β, etc.) that culminate in the elaborated expression of extracellular matrix proteins and irreversible injury. These results support a distinct pathobiol. role for atherogenic lipoproteins in the initiation and progression of cytokine-mediated renal injury.

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=> s l1 and lung () fibros?
        154838 LUNG
         39638 LUNGS
        168353 LUNG
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                (LUNG OR LUNGS)
          31786 FIBROS?
           1398 LUNG (W) FIBROS?
L10          13 L1 AND LUNG (W) FIBROS?

=> s l10 and review/dt
       1734424 REVIEW/DT
L11           2 L10 AND REVIEW/DT

=> d l11, ibib abs, 1-2

L11  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:         2001:583023  HCAPLUS
DOCUMENT NUMBER:          136:149208
TITLE:                    Cytokine related to pathogenesis of pulmonary fibrosis
AUTHOR(S):                Yasui, Masahide
CORPORATE SOURCE:         Graduate School of Medicine, Department of Cancer
                          Medicine, Kanazawa University, Japan
SOURCE:                   Molecular Medicine (Tokyo, Japan) (2001), 38(8),
                          886-892
                          CODEN: MOLMEL; ISSN: 0918-6557
PUBLISHER:                Nakayama Shoten
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 Japanese
AB   A review on roles of cytokines, chemokines, and growth factors in the
     pathogenesis of pulmonary fibrosis.  Development of pulmonary fibrosis and
     roles of inflammatory cytokines tumor necrosis factor-α, interleukin
     (IL)-1, and IL-6, chemokines IL-8, monocyte chemoattractant protein
     (MCP)-1, macrophage inflammatory protein (MIP)-1α, and MIP-2,
     and growth factors tumor growth factor (TGF)-β and platelet-derived
     growth factor (PDGF) are discussed.

L11  ANSWER 2 OF 2  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:         1998:436672  HCAPLUS
DOCUMENT NUMBER:          129:201256
TITLE:                    Regulation of lung fibrosis by cytokines
AUTHOR(S):                Ogushi, Fumitaka
CORPORATE SOURCE:         Third Department Internal Medicine, Tokushima
                          University, Tokushima, 770-8503, Japan
SOURCE:                   Kokyu (1998), 17(5), 587-594
                          CODEN: KOKUDH; ISSN: 0286-9314
PUBLISHER:                Respiration Research Foundation
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 Japanese
AB   A review with 61 refs.  Pulmonary fibrosis is thought to be the process of
     repairing damage after inflammation (alveolitis).  Cytokines produced from
     lung cells such as alveolar macrophages, lymphocytes, and fibroblasts,
     play an important role in the development of fibrosis.  These cytokines
     can be divided into several groups, namely, inflammatory cytokines
     including IL-1 and TNF-α, chemokines including IL-8 and MCP-1,
     and growth factors such as PDGF, TFG-β and IGF-1.  Inflammatory
     cytokines act in the process of alveolitis and growth factors act in the
     process of repair.  On the other hand, Th1 (IFN-γ) and Th2 (IL-4)
     cytokines have different regulatory effects on various functions of lung
     cells.  Th1 and Th2 cytokine imbalance is thought to be responsible for
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the pathogenesis of various diseases. In pulmonary fibrosis, Th1 cytokines may upregulate the inflammation and downregulate the process of fibrosis, whereas Th2 cytokines may downregulate the inflammation and upregulate the process of fibrosis. This paper summarizes the involvement of various cytokines and their regulation in the process of pulmonary fibrosis.

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=> s l1 and resten?
          5649 RESTEN?
L12         63 L1 AND RESTEN?

=> s l12 and review/dt
       1734424 REVIEW/DT
L13         12 L12 AND REVIEW/DT

=> d his

     (FILE 'HOME' ENTERED AT 19:25:27 ON 15 JUN 2004)

     FILE 'REGISTRY' ENTERED AT 19:25:35 ON 15 JUN 2004

     FILE 'HCAPLUS' ENTERED AT 19:25:39 ON 15 JUN 2004
L1          3461 S MCP-1
L2           110 S L1 AND INFLAMMAT? () DISEASE?
L3            14 S L2 AND REVIEW/DT
L4           117 S L1 AND RHEUMATOID? () ARTHRIT?
L5            11 S L4 AND REVIEW/DT
L6             9 S L5 NOT L3
L7             0 S L1 AND GLOMERULAR? () NEPHRITIDE?
L8           237 S L1 AND GLOMER?
L9            19 S L8 AND REVIEW/DT
L10           13 S L1 AND LUNG () FIBROS?
L11            2 S L10 AND REVIEW/DT
L12           63 S L1 AND RESTEN?
L13           12 S L12 AND REVIEW/DT

=> s l13 not l2
L14         10 L13 NOT L2

=> s l14 not l14
L15          0 L14 NOT L14

=> s l14 not l3
L16         10 L14 NOT L3

=> d l16, ibib abs, 1-10

L16  ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:        2004:5076  HCAPLUS
TITLE:                   Possible gene therapy of restenosis in the future
AUTHOR(S):               Kitamoto, Shiro; Egashira, Kensuke
CORPORATE SOURCE:        Graduate School of Medicine, Kyushu University, Japan
SOURCE:                  Bunshi Shin Kekkanbyo (2003), 4(6), 624-630
                         CODEN: BSKUAB; ISSN: 1345-2355
PUBLISHER:               Sentan Igakusha
DOCUMENT TYPE:           Journal; General Review
LANGUAGE:                Japanese
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AB A review, discussing possible gene therapy of **restenosis** in the future by targeting **MCP-1** and NF-κB mols.

L16 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:904519 HCAPLUS
DOCUMENT NUMBER: 140:331520
TITLE: Pharmacologic prevention of both **restenosis** and atherosclerosis progression: AGI-1067, probucol, statins, folic acid, and other therapies
AUTHOR(S): Tardif, Jean-Claude; Gregoire, Jean; Lavoie, Marc-Andre; L'Allier, Philippe L.
CORPORATE SOURCE: Department of Medicine, Montreal Heart Institute, Montreal, Can.
SOURCE: Current Opinion in Lipidology (2003), 14(6), 615-620
CODEN: COPLEU; ISSN: 0957-9672
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. In this article, the authors intend to provide an update on clin. trials of pharmacol. prevention of **restenosis** after percutaneous coronary interventions, placed in the perspective of the use of orally administered therapy for the prevention of atherosclerosis progression and clin. events. AGI-1067, the mono-succinic acid ester of probucol, is a phenolic antioxidant member of a novel class of agents termed v-protectants. It has strong antioxidant properties equipotent to those of probucol and antiinflammatory properties. It inhibits gene expression of VCAM-1 and **MCP-1** and was effective at preventing atherosclerosis in all tested animal models including the non-human primate. In the Canadian Antioxidant **Restenosis** Trial (CART) 1, AGI-1067 and probucol improved lumen dimensions at the site of percutaneous coronary intervention. AGI-1067 also improved luminal dimensions of non-intervened coronary ref. segments in the Canadian Antioxidant **Restenosis** Trial, which suggests a direct antiatherosclerosis effect. Probucol reduced post-percutaneous coronary intervention **restenosis** and progression of carotid atherosclerosis in other clin. trials. Although statins reduce atherosclerotic events, they do not appear to have a significant effect on **restenosis**. The failure of folate therapy to protect against **restenosis** in the Folate After Coronary Intervention Trial (FACIT) occurred despite significant redns. in Hcy levels. Prevention of both post-percutaneous coronary intervention **restenosis** and atherosclerosis progression with a pharmacol. agent such as AGI-1067 may be an attractive treatment paradigm. Two important trials that test the antioxidant/antiinflammatory hypothesis are ongoing with AGI-1067: the Canadian Atherosclerosis and **Restenosis** Trial 2, which assesses its value for the redn. of both atherosclerosis progression and post-percutaneous coronary interventions **restenosis**, and the Aggressive Redn. of Inflammation Stops Events (ARISE) trial which is evaluating its effects on cardiovascular events.
REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:803404 HCAPLUS
DOCUMENT NUMBER: 139:332165
TITLE: Anti-monocyte chemoattractant protein-1 gene therapy for cardiovascular diseases

AUTHOR(S): Kitamoto, Shiro; Egashira, Kensuke
CORPORATE SOURCE: Dep. of Cardiovascular Med., Grad. Sch. of Med. Sci., Kyushu Univ., 3-1-1, Maidashi, Higashi-ku, Fukuoka, 812-8582, Japan
SOURCE: Expert Review of Cardiovascular Therapy (2003), 1(3), 393-400
CODEN: ERCTAS; ISSN: 1477-9072
PUBLISHER: Future Drugs Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Recent studies have revealed that increased expression of monocyte chemoattractant protein (**MCP**)-**1** plays a central role in the pathogenesis of cardiovascular diseases. 7ND is the amino-terminal deletion mutant of human **MCP-1** and works as a dominant neg. inhibitor of **MCP-1**. We devised a new strategy of anti-**MCP-1** gene therapy by transfecting the 7ND gene into skeletal muscles. 7ND gene transfection suppressed arteriosclerotic changes induced by chronic inhibition of nitric oxide synthesis in rats and inhibited the development, progression and destabilization of atherosclerosis in apolipoprotein E knockout mice. This strategy also reduced **restenosis** after balloon injury in rats, rabbits and monkeys, and reduced neointimal formation after stent implantation in rabbits and monkeys. This new strategy can be a useful and feasible gene therapy against **MCP-1** related cardiovascular diseases.
REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2003:704642 HCAPLUS
DOCUMENT NUMBER: 139:285453
TITLE: AGI-1067: Treatment of atherosclerosis VCAM-1 and **MCP-1** expression inhibitor antioxidant
AUTHOR(S): Sorbera, L. A.; Castaner, J.
CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain
SOURCE: Drugs of the Future (2003), 28(5), 421-424
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. AGI-1067 is a monosuccinate ester of probucol that exhibited marked lipid-lowering and antioxidant activity. AGI-1067 potently inhibited VCAM-1 and **MCP-1** expression and smooth muscle cell proliferation and was effective in animal models of atherosclerosis and hyperlipidemia. The agent has shown efficacy in the prevention of atherosclerosis in patients with coronary artery disease and in preventing **restenosis** in patients undergoing percutaneous coronary interventions. AG-1067 is currently undergoing phase III trials with an indication for secondary prevention of atherosclerotic cardiovascular disease.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2003:281476 HCAPLUS
DOCUMENT NUMBER: 139:127233
TITLE: Anti-inflammatory therapeutic strategy against atherosclerosis and **restenosis** after coronary intervention

AUTHOR(S): Kitamoto, Shiro; Egashira, Kensuke; Takeshita, Akira
CORPORATE SOURCE: Department of Cardiovascular Medicine, Graduate School of Medical Science, Kyushu University, Fukuoka, 812-8582, Japan
SOURCE: Journal of Pharmacological Sciences (Tokyo, Japan) (2003), 91(3), 192-196
CODEN: JPSTGJ; ISSN: 1347-8613
PUBLISHER: Japanese Pharmacological Society
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Atherosclerosis and **restenosis** after percutaneous coronary interventions have become major issues in public health in Western countries. Recent studies have revealed that inflammation plays an important role in pathogenesis of cardiovascular diseases. Vascular injury may involve an inflammatory response, which accelerates the recruitment and activation of monocytes through monocyte chemoattractant protein-1 (**MCP-1**). **MCP-1** expression has been shown to be increased in atherosclerotic lesions and balloon injured arteries. Recently, we have devised a new strategy for anti-**MCP-1** gene therapy by transfecting mutant **MCP-1** gene into skeletal muscle. This mutant **MCP-1** has been shown to work as a dominant-neg. inhibitor of **MCP-1**. We here demonstrate that this strategy limited progression of pre-existing atherosclerotic lesions and improved the lesion compn. into a more stable phenotype in the hypercholesterolemic mice. This strategy also suppressed monocyte infiltration/activation in the injured site and markedly inhibited **restenotic** changes (neointimal hyperplasia) in the carotid artery in rabbits, rats, and monkeys after balloon injury or stent implantation. Therefore, **MCP-1**-mediated monocyte infiltration is essential in the development of **restenotic** changes as well as atherosclerosis progression. **MCP-1** can be a practical therapeutic target for human **restenosis** and atherosclerosis.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2003:169439 HCAPLUS
DOCUMENT NUMBER: 139:254517
TITLE: Translational research of gene therapy: **restenosis**
AUTHOR(S): Kitamoto, Shiro; Egashira, Kensuke
CORPORATE SOURCE: Department of Cardiovascular Medicine, Graduate School of Medical Sciences, Kyushu University, Fukuoka, 812-8582, Japan
SOURCE: Bunshi Shin Kekkanbyo (2003), 4(1), 26-33
CODEN: BSKUAB; ISSN: 1345-2355
PUBLISHER: Sentan Igakusha
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese
AB A review, discussing translational research on **MCP-1** for gene therapy of **restenosis**.

L16 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2003:151774 HCAPLUS
DOCUMENT NUMBER: 139:110891
TITLE: Molecular Mechanisms Mediating Inflammation in Vascular Disease
AUTHOR(S): Egashira, Kensuke

CORPORATE SOURCE: Graduate School of Medical Sciences, Department of Cardiovascular Medicine, Kyushu University, Fukuoka, Japan
SOURCE: Hypertension (2003), 41(3, Pt. 2), 834-841
CODEN: HPRTDN; ISSN: 0194-911X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. There are several clin. challenges for the treatment of intractable cardiovascular diseases, including **restenosis**, atherosclerotic complications resulting from plaque rupture, severe tissue ischemia, and heart failure. Emerging evidence suggests that an inflammatory process is involved in the pathogenesis of such intractable diseases. In particular, inflammatory responses to arterial injury, which cause continuous recruitment and activation of monocytes mainly through activation of the monocyte chemoattractant protein-1 (**MCP-1**) pathway, have a central role in **restenosis** and atherogenesis. We recently devised a new strategy for anti-**MCP-1** therapy by transfecting an N-terminal deletion mutant of the **MCP-1** gene into skeletal muscles. This mutant **MCP-1** lacks the N-terminal amino acids 2 to 8, called 7ND, and works as a dominant-neg. inhibitor of **MCP-1**. We demonstrated that 7ND gene transfer suppresses monocyte infiltration/activation after arterial injury and markedly inhibits exptl. **restenosis** in animals after balloon injury or stent placement. Furthermore, 7ND gene transfer not only attenuated the development of early atherosclerotic lesions but also limited progression of preexisting atherosclerotic lesions and changed the lesion compn. into a more stable phenotype in hypercholesterolemic mice. Vascular inflammation mediated by **MCP-1** might create a pos. feedback loop to enhance **restenotic** and atherosclerotic changes through activating lesional monocytes. Therefore, vascular inflammation mediated by **MCP-1** has a central role in the development of exptl. **restenosis**, atherosclerosis, and plaque destabilization, leading to acute coronary syndrome. This strategy for gene therapy might be useful against human **restenosis**, thereby opening a new therapeutic window for antirestenosis and antiatherosclerosis paradigms.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:100283 HCAPLUS
DOCUMENT NUMBER: 139:206805
TITLE: Gene therapy targeting monocyte chemoattractant protein-1 for vascular disease
AUTHOR(S): Kitamoto, Shiro; Egashira, Kensuke
CORPORATE SOURCE: Department of Cardiovascular Medicine, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
SOURCE: Journal of Atherosclerosis and Thrombosis (2002), 9(6), 261-265
CODEN: JATHEH; ISSN: 1340-3478
PUBLISHER: Japan Atherosclerosis Society
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Monocyte chemoattractant protein-1 (**MCP-1**) has been shown to play an essential role in the pathogenesis of arteriosclerosis and other vascular diseases, such as **restenosis** after arterial injury, by recruiting monocytes into the arterial wall. We devised a new strategy for anti-**MCP-1** gene therapy against arteriosclerosis by transfecting an amino-terminal deletion mutant (7ND), which lacks the amino-terminal

amino acids 2 to 8 of the human **MCP-1** gene, into a remote organ (skeletal muscles). I.m. transduction with the mutant **MCP-1** gene suppressed inflammatory and proliferative changes and arteriosclerosis formation induced by the chronic inhibition of nitric oxide synthesis in rats. 7ND gene transfection also inhibited the initiation, progression, and destabilization of atherosclerosis in Apolipoprotein E-knockout mice. Moreover, the strategy reduced **restenosis** after balloon injury in rabbits, rats, and monkeys, or neointimal formation after stent implantation in monkeys. This new strategy may be a useful and feasible gene therapy against atherosclerosis and **restenosis** after angioplasty.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:188799 HCAPLUS
DOCUMENT NUMBER: 134:339249
TITLE: Chemokines on the rise. **MCP-1** and **restenosis**
AUTHOR(S): Schmidt, Ann Marie; Stern, David M.
CORPORATE SOURCE: Departments of Surgery, Medicine, and Physiology and Cellular Biophysics, College of Physicans and Surgeons, Columbia University, New York, NY, USA
SOURCE: Arteriosclerosis, Thrombosis, and Vascular Biology (2001), 21(3), 297-299
CODEN: ATVBFA; ISSN: 1079-5642
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with 48 refs. on the role of monocyte chemoattractant protein 1 in the pathogenesis of vascular smooth muscle and mononuclear phagocyte activation and **restenosis**.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:653136 HCAPLUS
DOCUMENT NUMBER: 132:76442
TITLE: Flow-induced endothelial cell activation and gene regulation by mechanical forces
AUTHOR(S): Sprague, Eugene A.; Cayatte, Antonio J.; Nerem, Robert M.; Mohan, Sumathy
CORPORATE SOURCE: Department of Radiology, University of Texas Health Science Center at San Antonio, San Antonio, TX, 78284-7800, USA
SOURCE: Endothelial Cell Research Series (1999), 6(Mechanical Forces and the Endothelium), 189-206
CODEN: ECRSFY; ISSN: 1384-1270
PUBLISHER: Harwood Academic Publishers
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with 72 refs. This chapter examines the concept that flow patterns along the surface of the endothelium, like humoral mediators, can act either to enhance the typical antithrombogenic, tight junction endothelial phenotype or "activate" the endothelium in a manner analogous to the inflammatory cytokines. Moreover, this chapter puts forth the concept that the vascular endothelium exhibits a nonlinear response to fluid-imposed shear stress characterized by activation of vascular

endothelial cells at low shear levels (0.5-4 dynes/cm^2) relative to cells exposed to either no shear or shear levels exceeding 4 dynes/cm^2. Evidence supporting the stimulatory influence of low shear stress on monocyte-endothelial interaction and expression of **MCP-1** and VCAM-1 genes potentially involved in the recruitment and adhesion of blood monocytes to the endothelium is reviewed. The potential influence of low shear in mediating enhanced permeability of the arterial endothelium obsd. within arterial sites exposed to chronic low shear, reversing flow patterns is also discussed. Though much of the signal transduction pathway involved in transduction of the low shear signal into endothelial responses remains to be defined, evidence is presented indicating that longterm activation of the nuclear transcription factor, NF-κB, is obsd. in cultured human aortic endothelial cells exposed to prolonged low shear stress and that this pattern of response parallels that of enhanced VCAM-1 and **MCP-1** gene expression. In contrast, the influence of higher shear stress levels (12-15 dynes/cm^2) on endothelial cells to promote traits assocd. with a "healthy" endothelium are compared. Finally, the possible implications of low shear stress flow environments with regards to atherogenesis and **restenosis** are considered.

REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> s l1 and asthma
         24193 ASTHMA
            20 ASTHMAS
         24200 ASTHMA
                  (ASTHMA OR ASTHMAS)
L17          80 L1 AND ASTHMA

=> s l17 and review/dt
       1734424 REVIEW/DT
L18          10 L17 AND REVIEW/DT

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     (FILE 'HOME' ENTERED AT 19:25:27 ON 15 JUN 2004)

     FILE 'REGISTRY' ENTERED AT 19:25:35 ON 15 JUN 2004

     FILE 'HCAPLUS' ENTERED AT 19:25:39 ON 15 JUN 2004
L1          3461 S MCP-1
L2           110 S L1 AND INFLAMMAT? () DISEASE?
L3            14 S L2 AND REVIEW/DT
L4           117 S L1 AND RHEUMATOID? () ARTHRIT?
L5            11 S L4 AND REVIEW/DT
L6             9 S L5 NOT L3
L7             0 S L1 AND GLOMERULAR? () NEPHRITIDE?
L8           237 S L1 AND GLOMER?
L9            19 S L8 AND REVIEW/DT
L10           13 S L1 AND LUNG () FIBROS?
L11            2 S L10 AND REVIEW/DT
L12           63 S L1 AND RESTEN?
L13           12 S L12 AND REVIEW/DT
L14           10 S L13 NOT L2
L15            0 S L14 NOT L14
L16           10 S L14 NOT L3
L17           80 S L1 AND ASTHMA
L18           10 S L17 AND REVIEW/DT
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L19           8 L18 NOT L3

=> d l19, ibib abs, 1-8

L19  ANSWER 1 OF 8  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:          2003:896428  HCAPLUS
DOCUMENT NUMBER:           139:363148
TITLE:                     Stem cell factor: A hemopoietic cytokine with
                           important targets in asthma
AUTHOR(S):                 Oliveira, S. H. P.; Lukacs, N. W.
CORPORATE SOURCE:          Department of Basic Science, Aracatuba School of
                           Dentistry, State University of Sao Paulo, Aracatuba,
                           Brazil
SOURCE:                    Current Drug Targets: Inflammation & Allergy (2003),
                           2(4), 313-318
                           CODEN: CDTICU; ISSN: 1568-010X
PUBLISHER:                 Bentham Science Publishers Ltd.
DOCUMENT TYPE:             Journal; General Review
LANGUAGE:                  English
AB   We review evidence that Stem Cell Factor (SCF) plays an important role in
     the pathophysiol. of asthma. SCF is produced by a wide variety of cells
     present in asthmatic lung, including mast cells and eosinophils. Its
     receptor, c-kit, is broadly expressed on mature mast cells and
     eosinophils. SCF promotes recruitment of mast cell progenitors into
     tissues, as well as their local maturation and activation. It also
     promotes eosinophil survival, maturation and functional activation. SCF
     enhances IgE-dependent release of mediators from mast cells, including
     histamine, leukotrienes, cytokines (TNF-α, IL-5, GM-CSF) and
     chemokines (RANTES/CCL5, MCP-1/CCL2, TARC/CCL17 e MDC/CCL22); it is
     required for IL-4 prodn. in mast cells. SCF, acting in concert with IgE,
     also upregulates the expression and function of CC chemokine receptors in
     mast cells. Structural and resident airway cells express increased levels
     of SCF in the bronchus of asthmatic patients. In a murine model of
     asthma, allergen exposure increased prodn. of SCF by epithelial cells
     and alveolar macrophages, which was transient and paralleled by histamine
     release. SCF induced long-lived airway hyperreactivity, which was
     prevented by local neutralization of SCF, as well as by inhibitors of the
     prodn. or activity of cysteinyl-leukotrienes. Together, these
     observations suggest that SCF has an important role in asthma.
REFERENCE COUNT:           96    THERE ARE 96 CITED REFERENCES AVAILABLE FOR THIS
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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Full Text | Citing References

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ACCESSION NUMBER:          2003:521664  HCAPLUS
DOCUMENT NUMBER:           139:274520
TITLE:                     Significant Involvement of CCL2 (MCP-1) in
                           Inflammatory Disorders of the Lung
AUTHOR(S):                 Rose, C. Edward; Sung, Sung-Sang J.; Fu, Shu Man
CORPORATE SOURCE:          Division of Pulmunory and Critical Care Medicine and
                           the Division of Rheumatology and Immunology,
                           University of Virginia School of Medicine,
                           Charlottesville, VA, 22908, USA
SOURCE:                    Microcirculation (New York, NY, United States) (2003),
                           10(3/4), 273-288
                           CODEN: MROCER; ISSN: 1073-9688
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PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Mounting evidence suggests that CCL2 (**MCP-1**) and its hematopoietic cell receptor CC chemokine receptor 2 (CCR2) are involved in inflammatory disorders of the lung. In animal models of allergic **asthma**, idiopathic pulmonary fibrosis (IPF), and bronchiolitis obliterans syndrome (BOS), CCL2 expression and protein prodn. are increased and the disease process is attenuated by CCL2 immunoneutralization. Mechanisms by which CCL2 may be acting include recruitment of regulatory and effector leukocytes; stimulation of histamine or leukotriene release from mast cells or basophils; induction of fibroblast prodn. of transforming growth factor-β (TGF-β) and procollagen; and enhancement of Th2 polarization. Recently, polymorphism for CCL2 has been described with increased cytokine-induced release of CCL2 by monocytes and increased risk of allergic **asthma**. These studies identify potentially important roles for CCL2 in these lung inflammatory disorders. While CCL2 inhibition in patients with acute respiratory distress syndrome (ARDS) may be hazardous by interfering with defense against bacteremia, future studies are needed to det. if CCL2/CCR2 antagonism will offer breakthrough therapy for patients with allergic **asthma**, IPF, or BOS, and to confirm the hypothesis that CCL2 polymorphism places patients at greater risk for these disorders.
REFERENCE COUNT: 97 THERE ARE 97 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:158533 HCAPLUS
DOCUMENT NUMBER: 138:367164
TITLE: IL-17
AUTHOR(S): Hamuro, Junji
CORPORATE SOURCE: Japan
SOURCE: Biotherapy (Tokyo, Japan) (2003), 17(1), 85-97
CODEN: BITPE9; ISSN: 0914-2223
PUBLISHER: Gan to Kagaku Ryohosha
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese
AB A review. IL-17 is a potent proinflammatory cytokine produced mainly by activated memory CD4-T cells. The family of IL-17, a new family of cytokines, is composed of six functionally related members, ie, IL-17 and IL-17B-F in humans and mice. IL-17 exerts its biol. activity as a homodimer. In contrast to the selected expression pattern of this gene, the IL-17 receptor is ubiquitously distributed among diverse tissues and cells. IL-17 induces the secretion of IL-6, IL-8, PGE2, **MCP-1** and G-CSF by fibroblasts, keratinocytes, epithelial and endothelial cells, and is also able to induce ICAM-1 expression, T cell proliferation, and growth and differentiation of CD34+ human progenitors into neutrophils. The involvement of IL-17 in the rejection of allogeneic grafts has been demonstrated. The potent inflammatory actions that have been identified for IL-17 and the emerging assocns. with major human diseases, such as rheumatoid arthritis and allergic **asthma**, suggest that the family of IL-17 may have significant roles in the pathophysiol. of inflammatory processes. IL-17 induces prodn. of metalloproteinases and nitric oxide, responsible for the aggravation of arthritis and joint destruction. IL-17 can recruit and activate neutrophils in the airways, mediated by IL-8 and MIP-2. In addn., IL-17 stimulates human bronchial epithelial cells to release the neutrophil-activating factor IL-6.

L19 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:611630 HCAPLUS
DOCUMENT NUMBER: 137:350925
TITLE: Cytokines in chronic obstructive pulmonary disease
AUTHOR(S): Chung, K. F.
CORPORATE SOURCE: Natl. Heart & Long Inst., Imp. Coll. Sch. of Med., London, SW3 6LY, UK
SOURCE: European Respiratory Journal (2001), 18(Suppl. 34), 50S-59S
CODEN: ERJOEI; ISSN: 0903-1936
PUBLISHER: European Respiratory Society
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Chronic obstructive pulmonary disease (COPD) is characterized by chronic obstruction of expiratory flow affecting peripheral airways, assocd. with chronic bronchitis and emphysema, together with fibrosis and tissue damage, and inflammation of the small airways. Increased levels of interleukin (IL)-6, IL-1β, tumor necrosis factor-α (TNF-α) and IL-8 have been measured in sputum, with further increases during exacerbations, and the bronchiolar epithelium overexpresses monocyte chemotactic protein (**MCP**)-1 and IL-8. IL-8 can account for some chemotactic activity of sputum, and sputum IL-8 levels correlate with airway bacterial load and blood myeloperoxidase levels. The expression of chemokines such as RANTES may underlie the airway eosinophilia obsd. in some COPD patients. Cytokines may be involved in tissue remodelling. TNF-α and IL-1β stimulate macrophages to produce matrix metalloproteinase-9, and bronchial epithelial cells to produce extracellular matrix glycoproteins such as tenascin. Increased expression of transforming growth factor-β (TGFβ) and of epidermal growth factor (EGF) occurs in the epithelium and submucosal cells of patients with chronic bronchitis. TGFβ and EGF activate proliferation of fibroblasts, while activation of the EGF receptor leads to mucin gene expression. The cytokine profile seen in chronic obstructive pulmonary disease is different from that obsd. in **asthma**. There is a potential for anticytokine therapy in chronic obstructive pulmonary disease.

REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:354656 HCAPLUS
DOCUMENT NUMBER: 137:31703
TITLE: Cytokines and chemoattractants in allergic inflammation
AUTHOR(S): Romagnani, S.
CORPORATE SOURCE: Department of Internal Medicine, and Respiratory Diseases, Allergy, Section of Clinical Immunology, University of Florence, Florence, 50134, Italy
SOURCE: Molecular Immunology (2002), 38(12-13), 881-885
CODEN: MOIMD5; ISSN: 0161-5890
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. It is now generally accepted that type 2 T helper (Th2) cytokines and some chemoattractants play an essential role in the

pathogenesis of the allergic inflammation. The effects of Th2 cytokines, such as interleukin (IL)-4, IL-5, IL-9, and IL-13, account for virtually all the pathophysiol. manifestations of allergy and **asthma**. Moreover, both Th2 cells and the effector cells usually present in the areas of allergic inflammation (basophils, mast cells, and eosinophils) express chemoattractant receptors, such as CCR3, CCR4, CCR8, and CRTH2. Therefore, interactions of eotaxin(s), eotaxin/CCL11, RANTES/CCL5, and **MCP-1**/CCL2, MCP-2/CCL8, MCP-3/CCL7, MCP-4/CCL13 with CCR3 are responsible for the recruitment of basophils, eosinophils and mast cells, whereas interactions of CCR4 with MDC/CCL22 or TARC/CCL17, CCR8 with I-309/CCL1, and CRTH2 with PGD2 play a crit. role in the allergen-induced recruitment of Th2 cells in the target tissues of allergic inflammation. The demonstration that Th2-polarized responses against allergens represent the triggering event for the development of allergic diseases, together with the recognition that some chemoattractants are responsible for the recruitment of both Th2 cells and other effector cells of allergic inflammation, can provide the conceptual basis for the development of new therapeutic strategies in allergic conditions.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:136585 HCAPLUS
DOCUMENT NUMBER: 136:293048
TITLE: Chemokines in allergic lung inflammation
AUTHOR(S): Lloyd, Clare
CORPORATE SOURCE: Leukocyte Biology Section, Division of Biomedical Sciences, Faculty of Medicine, Imperial College of Science Technology and Medicine, London, SW7 2AZ, UK
SOURCE: Immunology (2002), 105(2), 144-154
CODEN: IMMUAM; ISSN: 0019-2805
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review discusses the role of chemokines in lung inflammation. Chemokines are potent chemoattractants and play a crit. role in directing inflammatory cell recruitment during pulmonary allergic inflammation. The actions of 3 particular CC chemokines, i.e., eotaxin, **MCP-1**, and macrophage-derived chemokine, are discussed. These chemokines are vital to the development of particular facets of the pathophysiol. assocd. with **asthma**. The role of chemokine has expanded to include maturation, differentiation, homing, activation and homeostatic trafficking of leukocytes within the immune system and in response to inflammation.

REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:509631 HCAPLUS
DOCUMENT NUMBER: 136:165494
TITLE: **MCP-1** and RANTES are mediators of acute and chronic inflammation
AUTHOR(S): Conti, P.; DiGioacchino, M.
CORPORATE SOURCE: Immunology Division, Department of Oncology and Neurosciences, School of Medicine, University of Chieti, Chieti, 66013, Italy
SOURCE: Allergy and Asthma Proceedings (2001), 22(3), 133-137

CODEN: AAPRFV; ISSN: 1088-5412
PUBLISHER: OceanSide Publications, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Regulation of leukocyte migration and activation by chemokines are recognized as potentially important functions in the induction of acute and chronic inflammatory reactions. Regulated upon activation normal T cell expressed and presumably secreted (RANTES), monocyte chemotactic protein-1 (**MCP-1**), and related mols. constitute the C-C class of the β chemokine supergene family with inflammatory properties. Here the authors report that in exptl. studies RANTES and **MCP-1** provoke mast cell activation and increase histidine decarboxylase mRNA expression in a dose-dependent manner. Moreover, injections of RANTES and **MCP-1** in the rat skin cause mast cell, eosinophil, and macrophage recruitment, and prostaglandin E2 generation. In a chronic inflammatory model **MCP-1** was found to mediate the recruitment of mononuclear cells in calcified granulomas. In addn., **MCP-1** mediated parasitic infections caused by Trichinella spiralis. In accordance with other studies, RANTES and **MCP-1** were found to play an important role in the lung allergic inflammation, lung leukocyte infiltration, bronchial hyperresponsiveness, and the recruitment of eosinophils in the pathogenesis of **asthma**. The authors propose a new mechanism of pulmonary airway inflammation where RANTES and **MCP-1** are deeply involved. The authors also studied the apparent role played by RANTES in the pathogenesis of relapsing-remitting multiple sclerosis enhancing the inflammatory response within the nervous system.

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:609087 HCAPLUS
DOCUMENT NUMBER: 131:335560
TITLE: Chemokines in inflammatory states
AUTHOR(S): Conti, P.; Barbacane, R. C.; Reale, M.
CORPORATE SOURCE: Immunology Division, Department of Oncology and Neurosciences, School of Medicine, University of Chieti, Chieti, 66013, Italy
SOURCE: Allergy and Asthma Proceedings (1999), 20(4), 205-208
CODEN: AAPRFV; ISSN: 1088-5412
PUBLISHER: OceanSide Publications, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB Chemokines probably mediate inflammation in **asthma** by acting on endothelial cells, alveolar cells, neutrophils, eosinophils, basophils, mast cells, monocytes, and lymphocytes, which are inhibited by corticosteroids. In 1995, the authors found that **MCP-1** provokes mast cell aggregation and [3H]5HT-release in cultured mast cells. In another study, **MCP-1** and RANTES revealed to have a potent chemoattractive effect on basophilic cells originating from the rat skin. In this inflammatory model, RANTES also attracted eosinophils and macrophages along with basophilic cells. The effect of RANTES on inducing HDC mRNA was dose dependent. **MCP-1** and RANTES provoked histamine release in intradermal mast cells and prostaglandin D2 generation. These effects clearly show that RANTES and **MCP-1** are mediators of acute inflammatory responses. In chronic inflammatory reactions, **MCP-1** is also present as we show in a study recently published by our group. In this paper, we found that **MCP-1**, strongly mediates the recruitment of mononuclear cells in the granuloma formed by KMnO4. In addn., **MCP-1** mediated a

parasitic infection caused by Trichinella spiralis in mice. Our data strongly demonstrate that chemokines, such as RANTES and **MCP-1**, mediate acute inflammatory response.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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10766 PSORIA?
L20 32 L1 AND PSORIA?

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1734424 REVIEW/DT
L21 1 L20 AND REVIEW/DT

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L21 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2003:891258 HCAPLUS
DOCUMENT NUMBER: 140:337383
TITLE: The role of chemokines in inflammatory skin diseases
AUTHOR(S): Girolomoni, G.; Pastore, S.; Cavani, A.; Albanesi, C.
CORPORATE SOURCE: Istituto Dermopatico dell' Immacolata, IRCCS, Rome, 00167, Italy
SOURCE: Ernst Schering Research Foundation Workshop (2004), 44(Leucocyte Trafficking), 191-225
CODEN: ESRWEL; ISSN: 0947-6075
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review on the role of chemokines in the development of inflammatory skin diseases. Chemokines appear to be crucial regulators of both the induction and expression of chronic inflammatory skin diseases. Allergic contact dermatitis (ACD) serves to be a valuable model for understanding the specific contribution of different T cell subsets as well as the mechanisms underlying the generation and regulation of T cell responses. The kinetics and pattern of chemokine expression during ACD resembles those obsd. during wound healing, IL-8 and **MCP-1** expressed first, followed by RANTES, finally by CXCR3 agonists, suggesting that the skin sets up a std. sequential pattern of chemokine expression in response to different types of injuries.
REFERENCE COUNT: 123 THERE ARE 123 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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182717 INFLAMM?
11625 BOWEL?
781585 DISEASE?
4185 INFLAMM? (W) BOWEL? (W) DISEASE?
L22 27 L1 AND INFLAMM? (W) BOWEL? (W) DISEASE?

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1734424 REVIEW/DT
L23 4 L22 AND REVIEW/DT

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     FILE 'REGISTRY' ENTERED AT 19:25:35 ON 15 JUN 2004

     FILE 'HCAPLUS' ENTERED AT 19:25:39 ON 15 JUN 2004
L1          3461 S MCP-1
L2           110 S L1 AND INFLAMMAT? () DISEASE?
L3            14 S L2 AND REVIEW/DT
L4           117 S L1 AND RHEUMATOID? () ARTHRIT?
L5            11 S L4 AND REVIEW/DT
L6             9 S L5 NOT L3
L7             0 S L1 AND GLOMERULAR? () NEPHRITIDE?
L8           237 S L1 AND GLOMER?
L9            19 S L8 AND REVIEW/DT
L10           13 S L1 AND LUNG () FIBROS?
L11            2 S L10 AND REVIEW/DT
L12           63 S L1 AND RESTEN?
L13           12 S L12 AND REVIEW/DT
L14           10 S L13 NOT L2
L15            0 S L14 NOT L14
L16           10 S L14 NOT L3
L17           80 S L1 AND ASTHMA
L18           10 S L17 AND REVIEW/DT
L19            8 S L18 NOT L3
L20           32 S L1 AND PSORIA?
L21            1 S L20 AND REVIEW/DT
L22           27 S L1 AND INFLAMM? () BOWEL? () DISEASE?
L23            4 S L22 AND REVIEW/DT

=> s l23 not l3
L24            4 L23 NOT L3

=> d l24, ibib abs, 1-4

L24  ANSWER 1 OF 4  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:         2001:457668  HCAPLUS
DOCUMENT NUMBER:          136:35947
TITLE:                    The pathogenesis of inflammatory bowel disease
                          viewed from immunological aspects
AUTHOR(S):                Hibi, Toshifumi; Inoue, Nagamu
CORPORATE SOURCE:         Dep. Internal Medicine, School Medicine, Keio Univ.,
                          Japan
SOURCE:                   Nippon Shokakibyo Gakkai Zasshi (2001), 98(4), 390-398
                          CODEN: NIPAA4; ISSN: 0446-6586
PUBLISHER:                Nippon Shokakibyo Gakkai
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 Japanese
AB   A review on immunopathogenesis of ulcerative colitis and Crohn's disease.
     T and B cell dysregulation and increased inflammatory cytokine and
     adhesion mol. expression in ulcerative colitis, abnormal
     monocyte/macrophage function, T cell dysregulation, enhanced prodn. of
     inflammatory and Th1 cytokines and chemokines interleukin-8 and MCP-1,
     and intestine-derived antigens in Crohn's disease, and animal models for
     inflammatory bowel disease are discussed.

L24  ANSWER 2 OF 4  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

ACCESSION NUMBER: 1999:724950 HCAPLUS
DOCUMENT NUMBER: 132:220916
TITLE: Chemokines in the **inflammatory bowel diseases**
AUTHOR(S): MacDermott, Richard P.
CORPORATE SOURCE: Division of Gastroenterology, The Albany Medical College, Albany, NY, 12208-3479, USA
SOURCE: Journal of Clinical Immunology (1999), 19(5), 266-272
CODEN: JCIMDO; ISSN: 0271-9142
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 47 refs. Ulcerative colitis and Crohn's disease are characterized by chronic intestinal inflammation. Intestinal bacteria initiate the activation of intestinal inflammatory processes, which are mediated by proinflammatory cytokines and chemokines. In **inflammatory bowel disease**, intestinal inflammation is not downregulated, in part due to defective or absent inhibitory processes. Studies to date have demonstrated that IL-8, **MCP-1**, and ENA-78 are highly expressed in the intestinal mucosa in areas of active Crohn's disease and ulcerative colitis. Neutrophils and macrophages in the inflamed intestine synthesize and secrete large amts. of chemokines in patients with **inflammatory bowel disease**. Increased chemokine expression has also been obsd. in epithelial cells, endothelial cells, and smooth muscle cells. Future trials of specific agents capable of inhibiting chemokine synthesis and secretion or blocking chemokine-chemokine receptor interaction will be important to study in patients with ulcerative colitis and Crohn's disease.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:547361 HCAPLUS
DOCUMENT NUMBER: 129:288800
TITLE: Cytokines in **inflammatory bowel disease**
AUTHOR(S): Kmiec, Zbigniew
CORPORATE SOURCE: Department of Histology and Immunology, University Medical School, Gdansk, 80-211, Pol.
SOURCE: Archivum Immunologiae et Therapiae Experimentalis (1998), 46(3), 143-155
CODEN: AITEAT; ISSN: 0004-069X
PUBLISHER: Ossolineum Publishing House
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 97 refs. **Inflammatory bowel disease** (IBD) denotes chronic inflammatory disorders of gastrointestinal tract of unknown etiol. that comprises 2 major groups: ulcerative colitis (UC) and Crohn's disease (CD). Dis-regulation of the intestinal immune system both at humoral and cellular level constitutes an important element in the multifactorial pathogenesis of IBD. The expression of pro-inflammatory cytokines, most notably IL-1, IL-6, TNF-α and chemokines (IL-8, ENA-78, **MCP-1**, RANTES) in intestinal mucosa from IBD patients is markedly enhanced, however, it is not always accompanied by increases in cytokines; serum levels. In IBD also significant changes occur in the tissue expression of immunoregulatory cytokines: increased levels of IL-2 mRNA and IFN-γ mRNA, and decreased expression of IL-4 were found in affected intestinal mucosa. Chronic intestinal lesions of patients with Crohn's disease are

assocd. with a Th1 type cytokine profile. The clin. effectiveness of anti-TNF-α antibodies and of IL-10 has been demonstrated in steroid-refractory Crohn's disease patients. The data demonstrating the role of cytokines in the pathogenesis of IBD should be carefully analyzed because of limitations imposed by the patient- and sample-related parameters. Further investigations will clarify the significance of the impairments in cytokine network for the initiation and progression of the IBD.

REFERENCE COUNT: 97 THERE ARE 97 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:87473 HCAPLUS
DOCUMENT NUMBER: 128:165969
TITLE: Chemokine production by intestinal epithelial cells: a therapeutic target in **inflammatory bowel disease**?
AUTHOR(S): Van Deventer, S. J. H.
CORPORATE SOURCE: Laboratory for Experimental Internal Medicine, Academic Medical Centre, Amsterdam, NL-1105 AZ, Neth.
SOURCE: Alimentary Pharmacology and Therapeutics (1997), 11(Suppl. 3), 116-121
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review and discussion with 37 refs. The intestinal epithelium plays an important role in the recognition of pathogenic organisms and in the recruitment of inflammatory cells to the mucosa. Epithelial chemokine prodn. may constitute a key target in future therapies for **inflammatory bowel disease** (IBD). Chemokines are divided into two subfamilies, the C-C family and C-X-C family. Most C-C chemokines target mononuclear cells and many C-X-C chemokines attract neutrophils. Interleukin-8 (IL-8), a C-X-C chemokine, acts as a motor for the recruitment of neutrophils into the non-inflamed mucosa and is present in both enterocytes and mucosal inflammatory cells. Epithelial cells may be the first to signal the presence of pathogens, as well as contributing to IL-8 prodn. in IBD. Data have also shown that intestinal epithelial cells are able to respond to IL-1β and tumor necrosis factor-alpha (TNF-α) at concns. known to occur in the inflamed mucosa. Monocyte chemotactic protein-1 (**MCP-1**), a member of the C-C chemokine family, is noticeably increased in IBD. These data show that C-X-C and C-C chemokines are equally important properties of mucosal epithelial cells. The effects of two anti-inflammatory drugs (dexamethasone and cyclosporin) on chemokine prodn. are significantly different and this provides a rationale for combination therapy.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> s l1 and mult? () scler?
        992936 MULT?
         31783 SCLER?
         10922 MULT? (W) SCLER?
L25         81 L1 AND MULT? (W) SCLER?

=> s l25 and review/dt
       1734424 REVIEW/DT
L26         12 L25 AND REVIEW/DT
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=> d his

     (FILE 'HOME' ENTERED AT 19:25:27 ON 15 JUN 2004)

     FILE 'REGISTRY' ENTERED AT 19:25:35 ON 15 JUN 2004

     FILE 'HCAPLUS' ENTERED AT 19:25:39 ON 15 JUN 2004
L1          3461 S MCP-1
L2           110 S L1 AND INFLAMMAT? () DISEASE?
L3            14 S L2 AND REVIEW/DT
L4           117 S L1 AND RHEUMATOID? () ARTHRIT?
L5            11 S L4 AND REVIEW/DT
L6             9 S L5 NOT L3
L7             0 S L1 AND GLOMERULAR? () NEPHRITIDE?
L8           237 S L1 AND GLOMER?
L9            19 S L8 AND REVIEW/DT
L10           13 S L1 AND LUNG () FIBROS?
L11            2 S L10 AND REVIEW/DT
L12           63 S L1 AND RESTEN?
L13           12 S L12 AND REVIEW/DT
L14           10 S L13 NOT L2
L15            0 S L14 NOT L14
L16           10 S L14 NOT L3
L17           80 S L1 AND ASTHMA
L18           10 S L17 AND REVIEW/DT
L19            8 S L18 NOT L3
L20           32 S L1 AND PSORIA?
L21            1 S L20 AND REVIEW/DT
L22           27 S L1 AND INFLAMM? () BOWEL? () DISEASE?
L23            4 S L22 AND REVIEW/DT
L24            4 S L23 NOT L3
L25           81 S L1 AND MULT? () SCLER?
L26           12 S L25 AND REVIEW/DT

=> s l26 not l3
L27           10 L26 NOT L3

=> d l27, ibib abs, 1-10

L27  ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:         2003:149671  HCAPLUS
DOCUMENT NUMBER:          138:285649
TITLE:                    Targeting monocyte chemoattractant protein-1
                          signalling in disease
AUTHOR(S):                Dawson, Janet; Miltz, Wolfgang; Mir, Anis K.;
                          Wiessner, Christoph
CORPORATE SOURCE:         Neurodegeneration Unit, Arthritis and Bone Metabolism
                          Research, Basel, CH-4002, Switz.
SOURCE:                   Expert Opinion on Therapeutic Targets (2003), 7(1),
                          35-48
                          CODEN: EOTTAO; ISSN: 1472-8222
PUBLISHER:                Ashley Publications Ltd.
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB    A review.  Monocyte chemoattractant protein-1 (MCP-1) has been
      implicated in many inflammatory and autoimmune diseases.  The
      G-protein-coupled receptor CCR-2B is probably the most important MCP-1
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receptor in vivo, and loss of **MCP-1** effector function alone is sufficient to impair monocytic trafficking in inflammation models. **MCP-1** signaling appears to be a relevant target, esp. in rheumatoid arthritis (RA). In RA patients, **MCP-1** is produced by synovial cells and infiltrating monocytes, plasma **MCP-1** concns. correlate with swollen joint count, and elevated serum **MCP-1** concns. were found in juvenile RA in patients with active disease. Modulation of **MCP-1** signaling in exptl. RA showed beneficial effects on inflammation and joint destruction. With respect to chronic neuroinflammation, a crit. role for **MCP-1** has been established in animal models for **multiple sclerosis**. In acute neuroinflammation, exptl. evidence for a detrimental role of **MCP-1** in stroke and excitotoxic injury has been found. Several selective small mol. wt. CCR-2B antagonists and **MCP-1**-blocking antibodies have been described. The proof for the validity of targeting **MCP-1** signaling in disease, however, has yet to be established in clin. trials.

REFERENCE COUNT: 156 THERE ARE 156 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:958245 HCAPLUS
DOCUMENT NUMBER: 138:302139
TITLE: The role of **MCP-1** (CCL2) and CCR2 in **multiple sclerosis** and experimental autoimmune encephalomyelitis (EAE)
AUTHOR(S): Mahad, Don J.; Ransohoff, Richard M.
CORPORATE SOURCE: The Lerner Research Institute, Department of Neurosciences, The Cleveland Clinic Foundation, Cleveland, OH, 44195, USA
SOURCE: Seminars in Immunology (2003), 15(1), 23-32
CODEN: SEIME2; ISSN: 1044-5323
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. **Multiple sclerosis** (MS) is the commonest inflammatory demyelinating disease of the human central nervous system (CNS). In MS, CNS inflammation is assocd. with demyelination and axonal degeneration, which leads to clin. presentation. Expression and cellular localization of CCL2/**MCP-1** and CCR2 in MS have been described in the three compartments: brain, cerebrospinal fluid (CSF) and blood. Evidence from descriptive, transgenic, knockout and neutralizing studies of exptl. autoimmune encephalomyelitis (EAE) points towards a nonredundant role of CCL2 and CCR2 in the recruitment of inflammatory infiltrate into the CNS. Hence, CCL2 and CCR2 may be targets for specific and effective treatment in MS.

REFERENCE COUNT: 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:619947 HCAPLUS
DOCUMENT NUMBER: 136:214989
TITLE: The pathogenesis of encephalitis
AUTHOR(S): Owens, Trevor; Tran, Elise H.; Hassan-Zahraee, Mina; Babcock, Alicia; Krakowski, Michelle L.; Fournier, Sylvie; Jensen, Michael B.; Finsen, Bente

CORPORATE SOURCE: Montreal Neurological Institute, Den.
SOURCE: Neuroimmune Biology (2001), 1(New Foundation of Biology), 387-397
CODEN: NBEIAQ; ISSN: 1567-7443
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review discussed the role of cytokine in encephalitis. One of the most fundamental neuroimmune interactions is that involving immune responses in and against the brain. Although the CNS is immunol.-privileged relative to other organs, activated T lymphocytes are known to cross the blood-brain barrier. Entry of virus-specific T cells, usually a host-protective event, can induce encephalitis. The pathol. of viral encephalitis is assocd. with inflammatory (Th1) immune responses against infected cells, such as in Theiler's virus infection of oligodendrocytes. Myelin reactivity can occur as a consequence of epitope spreading from anti-viral responses. Myelin-specific CD4+ T cells induce autoimmune encephalomyelitis. The inflammatory, demyelinating pathol. of exptl. autoimmune encephalomyelitis (EAE) is similar in many respects to that of **Multiple Sclerosis**, including axonal damage. We find that naive T cells can enter the CNS during EAE, and may become activated there if costimulator mols. such as B7 are expressed on MHC II+ microglia. Indeed, B7 is known to be induced by viral infection, thus linking infection to CNS autommunity. Although initiated by infiltrating T cells, many of the inflammatory mediators detected in the CNS in MS or EAE are produced by CNS-resident glial cells. Interferon-gamma (IFNγ), an immune cytokine not normally expressed in the adult CNS, can induce glial cells to produce a variety of mediators, including tumor necrosis factor (TNF) and nitric oxide, that are cytopathic for oligodendrocytes in vitro. TNF is also implicated in repair/regenerative responses, in vivo. We find that IFNγ amplified but did not affect the kinetics of microglial TNF prodn., induced in response to axonal lesioning in MBP promoter/IFNγ transgenic mice. TNF, whether induced by EAE or by axonal damage, was nevertheless produced in IFNγ-deficient mice. This indicates that there are endogenous programs of glial response, which are amplified by IFNγ. The macrophage-dominated, perivascular infiltrates that are characteristic of EAE were replaced by a disseminated, invasive neutrophilia in IFNγ-deficient mice, with lethal consequence. The EAE-assocd. enzyme NOS2, the cytokine interleukin-10, and chemokines **MCP-1** and RANTES were undetectable in IFNγ-deficient mice with EAE, whereas the neutrophil-attractant chemokines MIP2 and TCA3 became prominent. CNS glia may interact with immune cells via chemokines to redirect further infiltration. Restriction of NOS2 expression to parenchymal glia, in chimeric mice reconstituted with NOS2-/- bone marrow, conferred protection against EAE. Nitric oxide may play distinct roles when made by microglia/macrophages vs. astrocytes. Our observations demonstrate the capacity of the CNS to mediate and direct protective and inflammatory responses, and of the immune system to interpret and amplify CNS-derived signals.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:619925 HCAPLUS
DOCUMENT NUMBER: 136:214973
TITLE: Regulation of the immune response within the central nervous system

AUTHOR(S): Antel, Jack
CORPORATE SOURCE: Montreal Neurologic Institute, McGill University, Montreal, QC, Can.
SOURCE: Neuroimmune Biology (2001), 1(New Foundation of Biology), 87-98
CODEN: NBEIAQ; ISSN: 1567-7443
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. The human disease post vaccination (or acute disseminated) encephalomyelitis (ADEM) and its animal counterpart exptl. autoimmune encephalomyelitis (EAE) demonstrate that the CNS can be the selective target of a self-antigen directed immune response. These disorders are dependent on systemic CD4+ T cell sensitization to CNS antigens. In contrast to ADEM, the human disorder **multiple sclerosis** (MS), also postulated to reflect CNS directed immune responses, is characterized by its recurrent and or progressive disease course. The above clin. disorders raise issues regarding the role that resident cells of the CNS play in regulating CNS directed immune responses, under physiol. and pathol. conditions. Such participation could occur at the level of the blood brain barrier (BBB) and/or within the parenchyma of the CNS. BBB-lymphocyte interaction-the mol. events that regulate lymphocyte access to the CNS include those involved in adhesion, chemoattraction, and migration through the cellular and extracellular matrix components of the BBB. Using a Boyden chamber assay system as an in vitro model of lymphocyte migration, we could show an increased rate of migration of lymphocytes derived from MS patients compared to controls, through a barrier comprised either of fibronectin alone or of endothelial cells (EC) derived from adult human CNS microvessels. Migration could be partially inhibited by matrix metalloproteinase (MMP) inhibitors and antibodies to **MCP-1**, the major lymphocyte chemoattractant produced by the ECs. Although the ECs can be induced to express both MHC class II and co-stimulatory mols. (B7-1), they favor induction of T cell anergy rather than proliferation. The perivascular microglia are the fully functional antigen presenting cells (APCs) at the level of the BBB. Parenchymal cell-lymphocyte interactions-within the human adult CNS, microglia can express both MHC class II and co-stimulatory mols.; in vitro studies indicate their capacity to process and present antigen. In contrast, adult human astrocytes can be induced to express only MHC class II mols. They do not support classical antigen induced T cell proliferation but can support super-antigen induced responses. Parenchymal microglia are a source of the cytokine IL-12 that biases the T cell response toward a Th1 phenotype. In context of primary immune-mediated disease, the immune-glial cell network of interactive events is likely initiated by the former (e.g. via CD40-CD40L signaling). In context of neurodegenerative or chronic inflammatory CNS disorders, neural cells may play the central role in initiating or sustaining the response.
REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:509631 HCAPLUS
DOCUMENT NUMBER: 136:165494
TITLE: **MCP-1** and RANTES are mediators of acute and chronic inflammation
AUTHOR(S): Conti, P.; DiGioacchino, M.
CORPORATE SOURCE: Immunology Division, Department of Oncology and Neurosciences, School of Medicine, University of

Chieti, Chieti, 66013, Italy
SOURCE: Allergy and Asthma Proceedings (2001), 22(3), 133-137
CODEN: AAPRFV; ISSN: 1088-5412
PUBLISHER: OceanSide Publications, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Regulation of leukocyte migration and activation by chemokines are recognized as potentially important functions in the induction of acute and chronic inflammatory reactions. Regulated upon activation normal T cell expressed and presumably secreted (RANTES), monocyte chemotactic protein-1 (**MCP-1**), and related mols. constitute the C-C class of the β chemokine supergene family with inflammatory properties. Here the authors report that in exptl. studies RANTES and **MCP-1** provoke mast cell activation and increase histidine decarboxylase mRNA expression in a dose-dependent manner. Moreover, injections of RANTES and **MCP-1** in the rat skin cause mast cell, eosinophil, and macrophage recruitment, and prostaglandin E2 generation. In a chronic inflammatory model **MCP-1** was found to mediate the recruitment of mononuclear cells in calcified granulomas. In addn., **MCP-1** mediated parasitic infections caused by Trichinella spiralis. In accordance with other studies, RANTES and **MCP-1** were found to play an important role in the lung allergic inflammation, lung leukocyte infiltration, bronchial hyperresponsiveness, and the recruitment of eosinophils in the pathogenesis of asthma. The authors propose a new mechanism of pulmonary airway inflammation where RANTES and **MCP-1** are deeply involved. The authors also studied the apparent role played by RANTES in the pathogenesis of relapsing-remitting **multiple sclerosis** enhancing the inflammatory response within the nervous system.
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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Full Text | Citing References

ACCESSION NUMBER: 2000:903438 HCAPLUS
DOCUMENT NUMBER: 135:75353
TITLE: Chemokines and chemokine receptors in inflammation of the nervous system: Manifold roles and exquisite regulation
AUTHOR(S): Huang, DeRen; Han, Yulong; Rani, M. R. Sandhya; Glabinski, Andrzej; Trebst, Corinna; Sorensen, Torben; Tani, Marie; Wang, Jintang; Chien, Phil; O'Bryan, Sage; Bielecki, Bartosz; Zhou, Zhihong Lucy; Majumder, Sarmila; Ransohoff, Richard M.
CORPORATE SOURCE: Departments of Neurology and Neurosciences and The Lerner Research Institute, The Cleveland Clinic Foundation, Cleveland, OH, 44195, USA
SOURCE: Immunological Reviews (2000), 177, 52-67
CODEN: IMRED2; ISSN: 0105-2896
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with 119 refs. focusing on the prodn. of chemokines by resident glial cells of the nervous system. The authors describe studies in 2 distinct categories of inflammation within the nervous system: immune-mediated inflammation as seen in exptl. autoimmune encephalomyelitis (EAE) or **multiple sclerosis** (MS) and post-traumatic inflammation. They provide evidence that chemokines play a role in amplifying the inflammatory reaction in EAE (and, probably, MS). In the context of neural trauma, chemokines appear to be primary stimuli for

leukocyte recruitment. Strikingly, expression of monocyte chemoattractant protein (**MCP**)-**1** and interferon-γ-inducible protein-10 (IP-10) are largely restricted to astrocytes or other glial cells in these diverse pathol. states. The remainder of the review focuses on studies that address the mol. mechanisms which underlie transcriptional regulation of 3 astrocyte-derived chemokines: **MCP-1**, IP-10, and β-R1/interferon-γ-inducible T-cell chemoattractant (I-TAC). Based on these studies, the authors propose that the complex promoters of these genes are marvelously organized for flexible and efficient response to challenge. In the case of **MCP-1**, several different stimuli can elicit gene transcription, acting through a conserved mechanism that includes binding of inducible transcription factors and recruitment of the constitutive factor Sp1. For IP-10 and β-R1/I-TAC, it appears that efficient gene transcription occurs only in highly inflammatory circumstances that produce aggregates of simultaneous stimuli. These characteristics, in turn, mirror the expression patterns of the endogenous genes: **MCP-1** is expressed under a variety of circumstances, while IP-10 appears primarily during immune-mediated processes that feature exposure of resident neuroglia to high levels of inflammatory cytokines.

REFERENCE COUNT: 119 THERE ARE 119 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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Full Text | Citing References

ACCESSION NUMBER: 2000:396379 HCAPLUS
DOCUMENT NUMBER: 133:162753
TITLE: Cytokine therapy in immune-mediated demyelinating diseases of the central nervous system: a novel gene therapy approach
AUTHOR(S): Martino, G.; Poliani, P. L.; Furlan, R.; Marconi, P.; Glorioso, J. C.; Adorini, L.; Comi, G.
CORPORATE SOURCE: Experimental Neuroimmunotherapy Unit, DIBIT-San Raffaele Scientific Institute, Milan, 20132, Italy
SOURCE: Journal of Neuroimmunology (2000), 107(2), 184-190
CODEN: JNRIDW; ISSN: 0165-5728
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 37 refs. Pro-inflammatory cytokines play a crucial role in the regulatory and effector phase of the immune-mediated mechanism sustaining **multiple sclerosis** pathogenesis (MS) thus supporting the use of anti-inflammatory cytokines as a therapeutic option. Systemic administration of cytokines shows, however, limited therapeutic efficacy and undesirable/unpredictable side-effects. The authors have developed a non-toxic system to deliver cytokines within the central nervous system (CNS) based on the intrathecal (i.c.) administration of non-replicative herpes simplex (HSV) type-1-derived viral vectors engineered with heterologous cytokine genes. Compared to controls, mice affected by exptl. autoimmune encephalomyelitis (EAE) and i.c. injected with an HSV-1-derived vector contg. the gene of the anti-inflammatory cytokine IL-4 showed a significant amelioration of clin. and pathol. EAE signs. A decreased mRNA expression of the monocyte chemoattractant protein-1 (**MCP-1**) by mononuclear CNS-infiltrating cells was also obsd. Peripheral T cells from IL-4-treated mice were not affected both in their antigen-specific proliferative response and in the cytokine secretion pattern. The authors' results indicate that CNS cytokine delivery with HSV-1-derived vectors is a feasible therapeutic strategy and might

represent an alternative approach for the treatment of immune-mediated demyelinating diseases. Advantages of this approach over systemic cytokine administration are the high cytokine level reached within the CNS and the absence of side-effects on the peripheral immune system. The short-lasting cytokine prodn. in the CNS after a single vector administration (4 wk) is the limiting factor of this novel technol. which, although promising, has to be improved.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:233070 HCAPLUS
DOCUMENT NUMBER: 132:263760
TITLE: Chemokines as mediators for intercellular communication in the brain
AUTHOR(S): Minami, Masabumi; Satoh, Masamichi
CORPORATE SOURCE: Dep. Mol. Pharmacol., Fac. Pharm. Sci., Kyoto Univ., Kyoto, 606-8501, Japan
SOURCE: Nippon Yakurigaku Zasshi (2000), 115(4), 193-200
CODEN: NYKZAU; ISSN: 0015-5691
PUBLISHER: Nippon Yakuri Gakkai
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese

AB A review with 40 refs. Chemokines constitute a large and still growing family of structurally-related small (8-10 kDa) cytokines that have chemotactic activity for leukocytes. Recently, some receptors for chemokines were reported to be used as a co-receptor by HIV at infection. In addn. to their well-established role in inflammatory response and recently-reported role as a co-receptor for HIV, recent data suggest that chemokines and their receptors physiol. and pathol. play crucial roles as the mediators for intercellular communication among the cells intrinsic to and recruited into the brain; i.e., neurons, astrocytes, microglia, endothelial cells, and leukocytes. Some chemokines such as SDF-1 and fractalkine are constitutively produced in the brain, implicating that they have an important role in maintenance of CNS homeostasis ro detn. of the patterning of neurons and/or glial cells in developing brain and normal adult brain. Chemokines such as **MCP-1**, MIP-1α, and CINC were shown to be induced by various neuroinflammatory stimuli, suggesting that they are involved in various neurodegenerative diseases such as **multiple sclerosis**, Alzheimer's disease, stroke, and AIDS dementia syndrome. Chemokines and their receptors are potential targets for therapeutic intervention in neurodegenerative diseases.

L27 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:252692 HCAPLUS
DOCUMENT NUMBER: 129:53105
TITLE: Chemokines and chemotaxis of leukocytes in infectious meningitis
AUTHOR(S): Lahrtz, Fritz; Piali, Luca; Spanaus, Katharina-Susanne; Seebach, Jorg; Fontana, Adriano
CORPORATE SOURCE: Department of Internal Medicine, Section of Clinical Immunology, University Hospital, Zurich, 8044, Switz.
SOURCE: Journal of Neuroimmunology (1998), 85(1), 33-43
CODEN: JNRIDW; ISSN: 0165-5728
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: English

AB A review with more than 100 refs. Chemokines constitute a constantly growing family of small inflammatory cytokines. They have been implied in many different diseases of the CNS including trauma, stroke and inflammation, e.g., **multiple sclerosis**. In this review we focus on the role of chemokines in infectious meningitis of bacterial or viral origin. In exptl. bacterial meningitis induced by Listeria monocytogeneses both CXC and CC chemokines namely MIP-1α, MIP-1β and MIP-2 are produced intrathecally by meningeal macrophages and leukocytes which infiltrate into the CNS. In patients with bacterial meningitis, IL-8, GROα, **MCP-1**, MIP-1α and MIP-1β are detectable in the CSF. These chemokines contribute to CSF mediated chemotaxis of neutrophils and PBMC in vitro. In viral meningitis IL-8, IP-10 and **MCP-1** are identified in the CSF to be responsible for chemotactic activity on neutrophils, PBMC and activated T cells. Taken collectively these data indicate that the recruitment of leukocytes in infectious meningitis involves the intrathecal prodn. of chemokines.

REFERENCE COUNT: 114 THERE ARE 114 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:260381 HCAPLUS

DOCUMENT NUMBER: 126:315564

TITLE: Neurotrophins and their receptors in nerve injury and repair

AUTHOR(S): Ebadi, M.; Bashir, R. M.; Heidrick, M. L.; Hamada, F. M.; El Refaey, H.; Hamed, A.; Helal, G.; Baxi, M. D.; Cerutis, D. R.; Lassi, N. K.

CORPORATE SOURCE: Dep. Pharmacology, Univ. Nebraska College Med., Omaha, NE, 68198-6260, USA

SOURCE: Neurochemistry International (1997), 30(4/5), 347-374
CODEN: NEUIDS; ISSN: 0197-0186

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: English

AB A review with 251 refs. Cytokines are a heterogeneous group of polypeptide mediators that have been assocd. with activation of numerous functions, including the immune system and inflammatory responses. The cytokine families include, but are not limited to, interleukin (IL-1α, IL-1β, IL-1ra and IL-2-IL-15), chemokines (IL-8/NAP-1, NAP-2, MIP-1α and β, MCAF/**MCP-1**, MGSA and RANTES), tumor necrosis factors (TNF-α and TNF-β), interferons (IFN-α, β and γ), colony stimulating factors (G-CSF, M-CSF, GM-CSF, IL-3 and some of the other ILs), growth factors (EGF, FGF, PDGF, TGFα, TGFβ and ECGF), neuropoietins (LIF, CNTF< OM and IL-6), and neurotrophins (BDNF, NGF, NT-3-NT-6 and GDNF). The neurotrophins represent a family of survival and differentiation factors that exert profound effects in the central and peripheral nervous system (PNS). The neurotrophins are currently under investigation as therapeutic agents for the treatment of neurodegenerative disorders and nerve injury either individually or in combination with other trophic factors such as ciliary neurotrophic factor (CNTF) or fibroblast growth factor (FGF). Responsiveness of neurons to a given neurotrophin is governed by the expression of two classes of cell surface receptor. For nerve growth factor (NGF), these are p75NTR (p75) and p140trk (referred to as trk or trkA), which binds both BDNF and neurotrophin (NT)-4/5, and trkC receptor,

which binds only NT-3. After binding ligand, the neurotrophin-receptor complex is internalized and retrogradely transported in the axon to the soma. Both receptors undergo ligand-induced dimerization, which activates multiple signal transduction pathways. These include the ras-dependent pathway utilized by trk to mediate neurotrophin effects such as survival and differentiation. Indeed, cellular diversity in the nervous system evolves from the concerted processes of cell proliferation, differentiation, migration, survival, and synapse formation. Neural adhesion and extracellular matrix mols. have been shown to play crucial roles in axonal migration, guidance, and growth cone targeting. Proinflammatory cytokines, released by activated macrophages and monocytes during infection, can act on neural targets that control thermogenesis, behavior, and mood. In addn. to induction of fever, cytokines induce other biol. functions assocd. with the acute phase response, including hypophagia and sleep. Cytokine prodn. has been detected within the central nervous system as a result of brain injury, following stab wound to the brain, during viral and bacterial infections (AIDS and meningitis), and in neurodegenerative processes (**multiple sclerosis** and Alzheimer's disease)1. Novel cytokine therapies, such as anti-cytokine antibodies or specific receptor antagonists acting on the cytokine network may provide an optimistic feature for treatment of **multiple sclerosis** and other diseases in which cytokines have been implicated.

REFERENCE COUNT: 251 THERE ARE 251 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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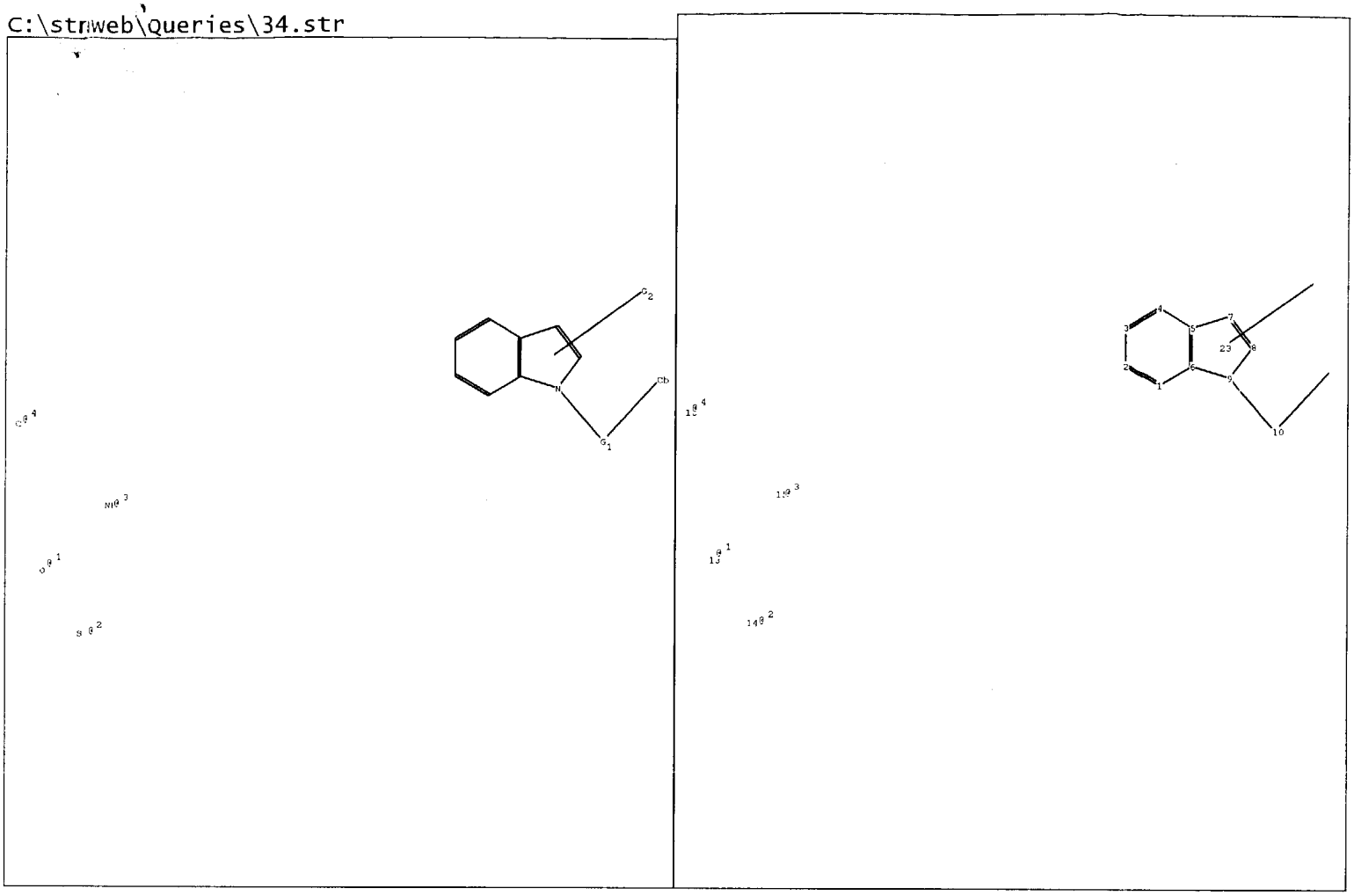

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ring nodes :
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ring bonds :
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exact/norm bonds :
    6-9  8-9  9-10  10-12
exact bonds :
    5-7  7-8
normalized bonds :
    1-2  1-6  2-3  3-4  4-5  5-6
isolated ring systems :
    containing 1 :


G1:C,SO2

G2:[*1],[*2],[*3],[*4]

Match level :
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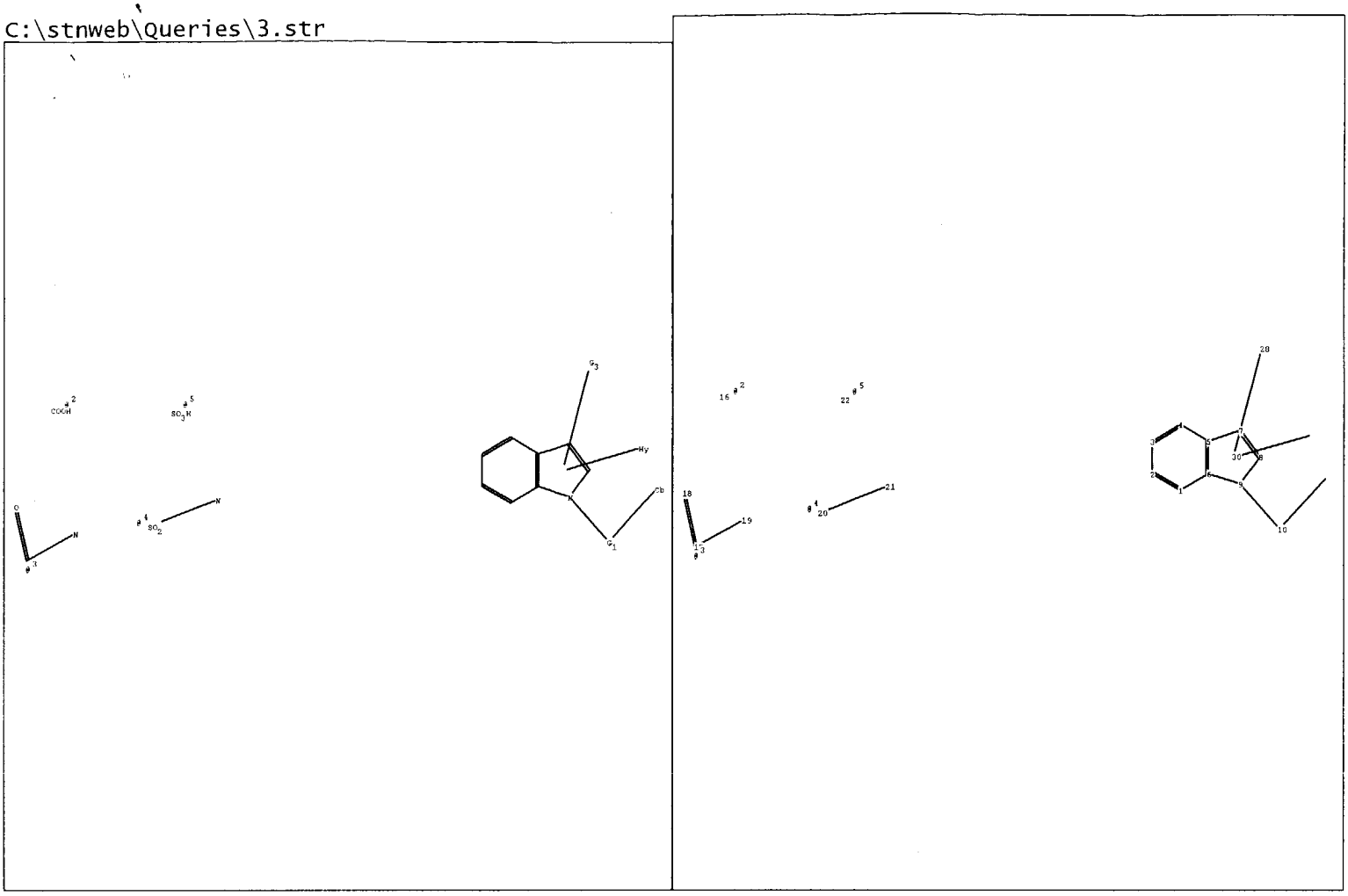

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ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
9-10 10-12 17-18 17-19 20-21
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9
exact/norm bonds :
6-9 8-9 9-10 10-12 17-18 17-19 20-21
exact bonds :
5-7 7-8
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :

G1:C,SO2

G2

G3:[*2],[*3],[*4],[*5]

Match level :
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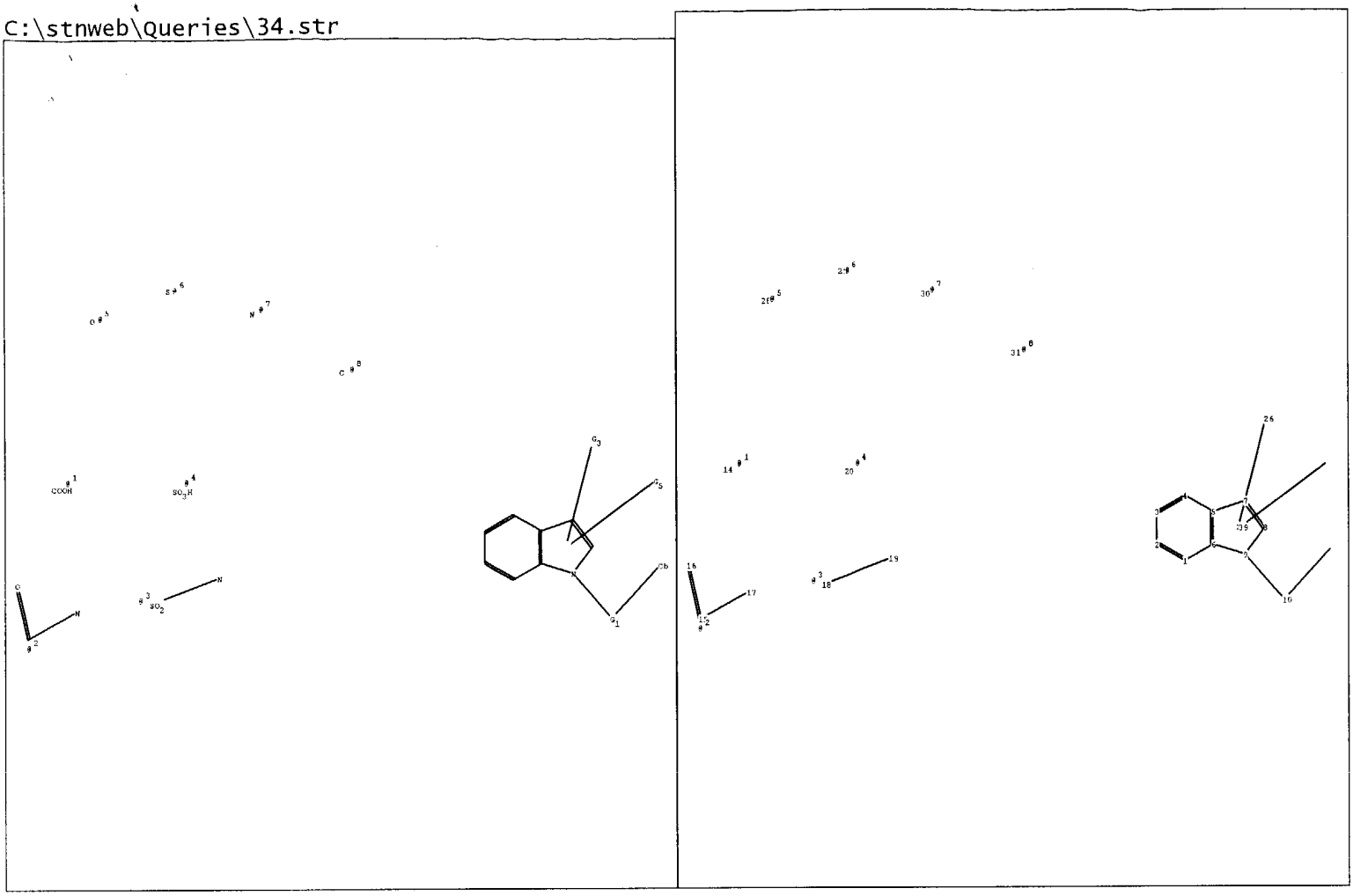

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ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
9-10 10-12 15-16 15-17 18-19
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9
exact/norm bonds :
6-9 8-9 9-10 10-12 15-16 15-17 18-19
exact bonds :
5-7 7-8
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :

G1:C,SO2

G3:[*1],[*2],[*3],[*4]

G4:[*1],[*2],[*3],[*4],[*5],[*6],[*7],[*8]

G5:[*5],[*6],[*7],[*8]

Match level :
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28:CLASS 29:CLASS 30:CLASS 31:CLASS 38:CLASS 39:CLASS

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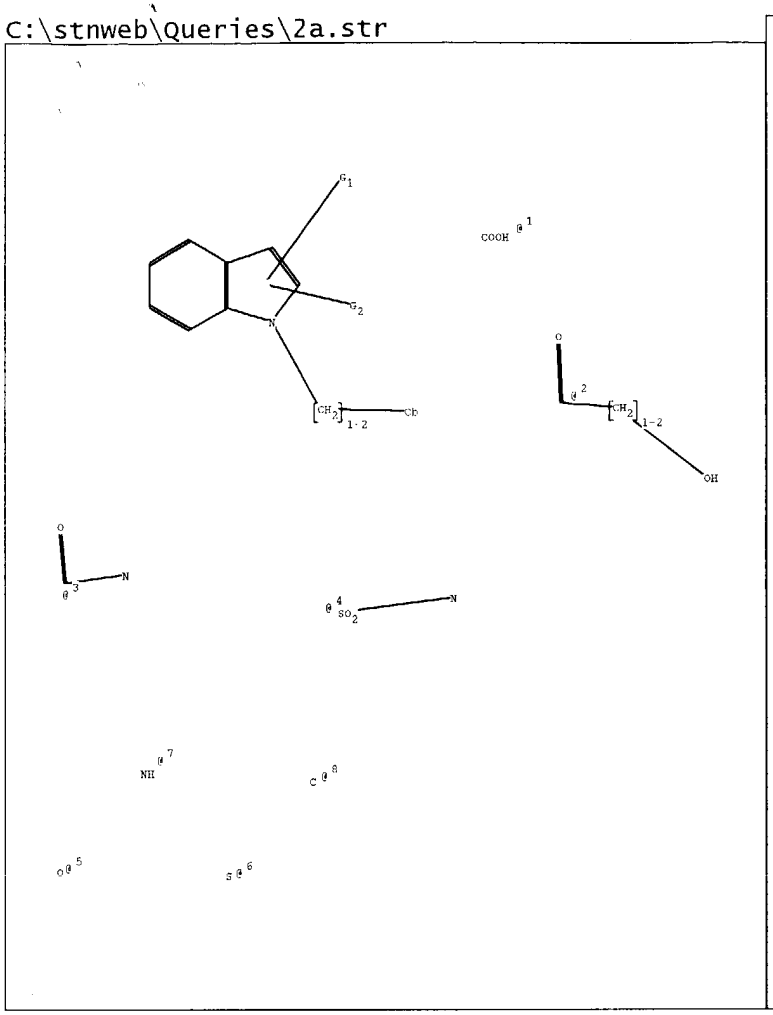

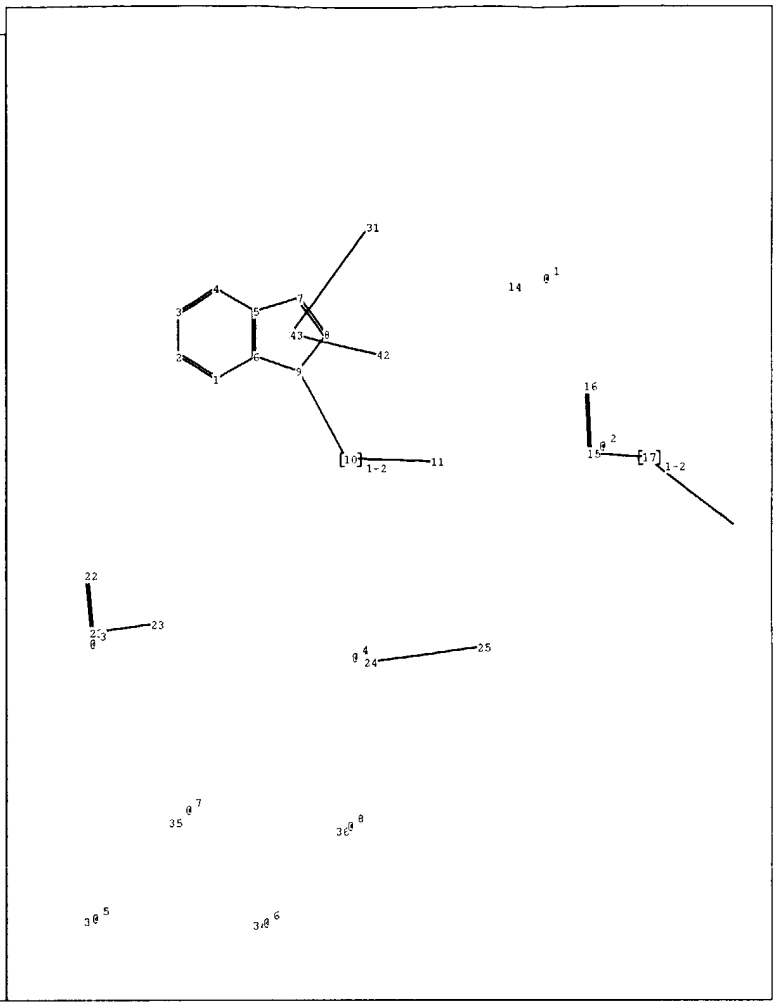

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ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
9-10 10-11 15-16 15-17 17-18 21-22 21-23 24-25
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9
exact/norm bonds :
6-9 8-9 15-16 21-22 21-23 24-25
exact bonds :
5-7 7-8 9-10 10-11 15-17 17-18
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :

G1:[*1],[*2],[*3],[*4]

G2:[*5],[*6],[*7],[*8]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS 11:Atom
14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS
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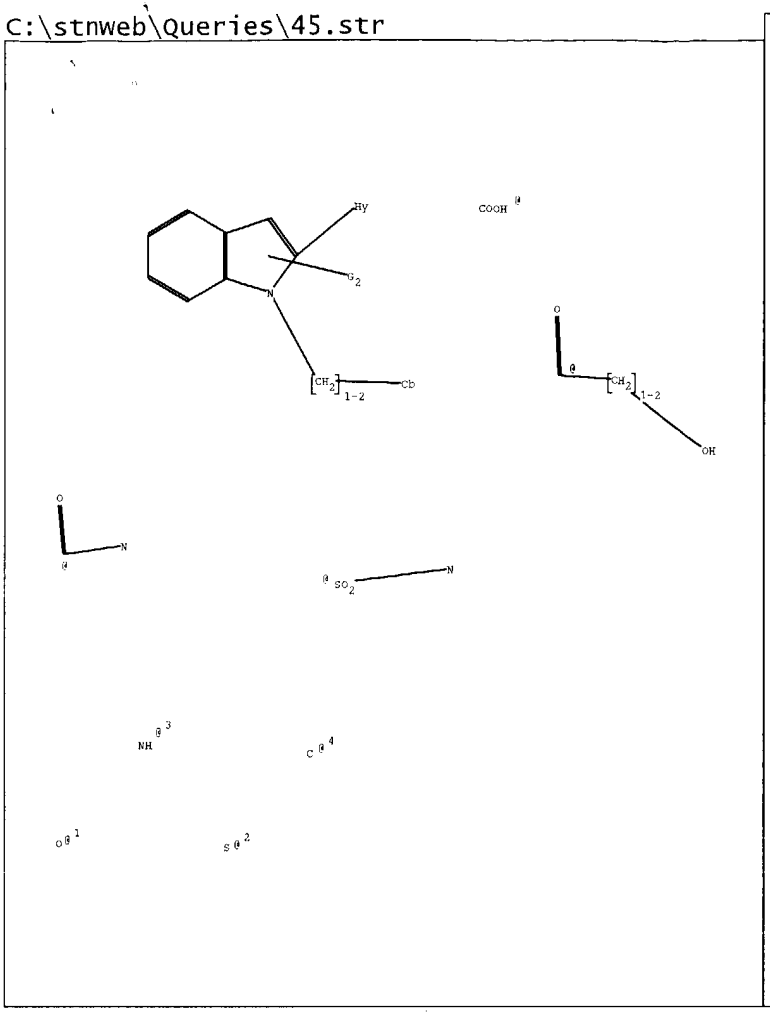

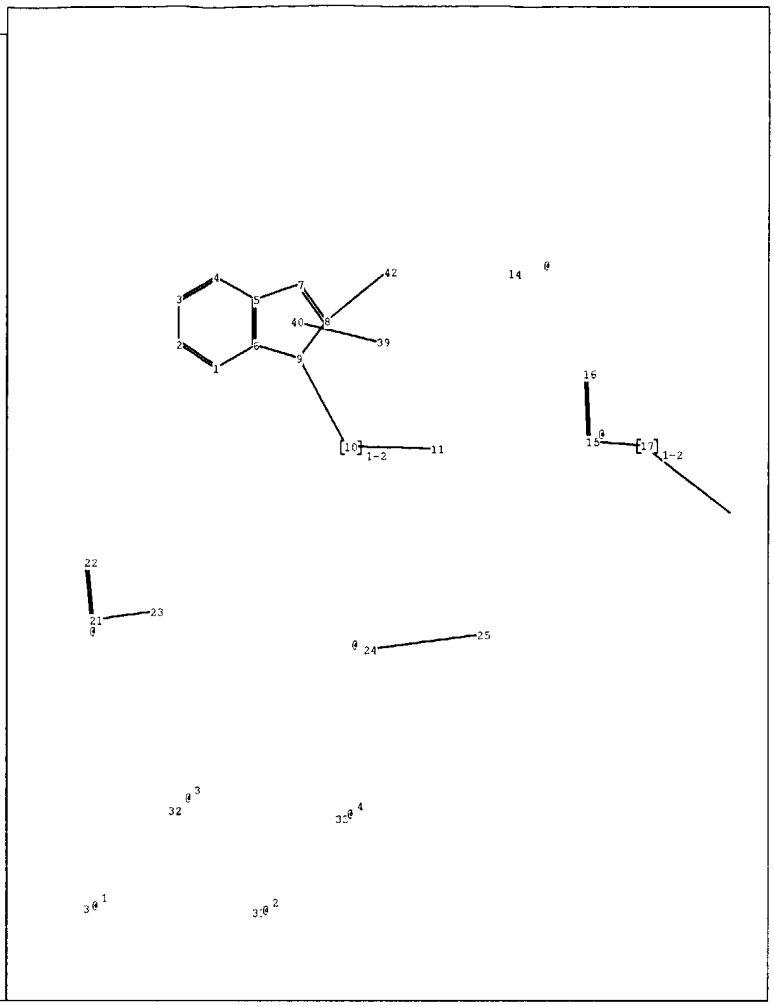

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10 11 14 15 16 17 18 21 22 23 24 25 30 31 32 33 39 42
ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
8-42 9-10 10-11 15-16 15-17 17-18 21-22 21-23 24-25
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9
exact/norm bonds :
6-9 8-9 8-42 15-16 21-22 21-23 24-25
exact bonds :
5-7 7-8 9-10 10-11 15-17 17-18
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :

G2:[*1],[*2],[*3],[*4]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS 11:Atom
14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS
25:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 39:CLASS 40:CLASS 42:CLASS

Session text above this point is available in the transcript, available from the **Transcript Assistant** on the toolbar.

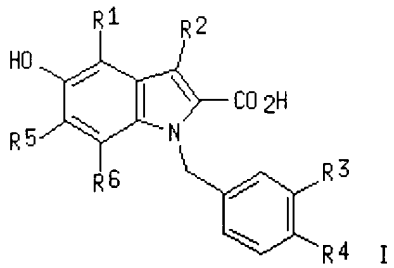
Full Text | Citing References

ACCESSION NUMBER: 2001:526057 HCAPLUS
DOCUMENT NUMBER: 135:107248
TITLE: Preparation of indole-2-carboxylic acids as MCP-1 receptor antagonists
INVENTOR(S): Faull, Alan Wellington; Kettle, Jason Grant
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001051466	A1	20010719	WO 2001-GB69	20010111
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2001007404	A	20021008	BR 2001-7404	20010111
EP 1252142	A1	20021030	EP 2001-900494	20010111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003519683	T2	20030624	JP 2001-551848	20010111
EE 200200394	A	20031215	EE 2002-394	20010111
BG 106894	A	20030430	BG 2002-106894	20020702
US 2003144339	A1	20030731	US 2002-169717	20020709
NO 2002003380	A	20020903	NO 2002-3380	20020712

PRIORITY APPLN. INFO.: GB 2000-626 A 20000113
WO 2001-GB69 W 20010111

OTHER SOURCE(S): MARPAT 135:107248
GI



I

AB The title compds. [I; R1 = H, halo, OMe; R2 = H, halo, Me, Et, OMe; R3 =

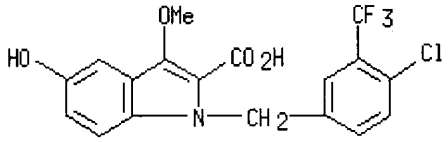
halo, CF3; R4 = halo, CF3; R5 = H, halo; R6 = H, halo; provided that when R5 and R6 are both H atom, and one of R3 or R4 is Cl or F, then the other is not Cl or F] and their prodrugs which have useful activity for the treatment of **inflammatory** disease, specifically in antagonizing an MCP-1 mediated effect in a warm-blooded animal such as a human being, were prepd. and formulated. Thus, reacting Et N-(3-trifluoromethyl 4-chlorobenzyl)-5-acetoxyindole-2-carboxylate (prepn. given) with NaOH in H2O/MeOH followed by treatment with 2M HCl afforded 71% I [R1, R2, R5, R6 = H; R3 = CF3; R4 = Cl]. The tested compds. I had IC50's of ≤ 50 μM in the hMCP-1 receptor binding assay.

IT **350596-52-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of indole-2-carboxylic acids as MCP-1 receptor antagonists)

RN 350596-52-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[[4-chloro-3-(trifluoromethyl)phenyl]methyl]-5-hydroxy-3-methoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:319722 HCAPLUS
DOCUMENT NUMBER: 134:320871
TITLE: Pharmaceuticals for treating obesity containing antagonists and partial agonists of PPAR-γ
INVENTOR(S): Berger, Joel P.; Doebber, Thomas W.; Leibowitz, Mark; Moller, David E.; Mosley, Ralph T.; Tolman, Richard L.; Ventre, John; Zhang, Bei B.; Zhou, Gaochao
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001030343	A1	20010503	WO 2000-US28924	20001019
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1284728	A1	20030226	EP 2000-973670	20001019

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

JP 2003525217	T2	20030826	JP 2001-532763		20001019
US 2003032581	A1	20030213	US 2002-241106		20020911
PRIORITY APPLN. INFO.:			US 1999-161225P	P	19991022
			US 2000-691955	A3	20001019
			WO 2000-US28924	W	20001019

OTHER SOURCE(S): MARPAT 134:320871

AB Compds. which are antagonists of strong PPAR-γ agonists, such as rosiglitazone, and are also partial agonists of the PPAR-γ receptor, are active agents for correcting or reducing obesity. For example, 1-(p-chlorobenzyl)-5-chloro-3-thiophenylindole-2-carboxylic acid, is characterized as being a potent and selective ligand for PPAR-γ which has partial agonist (<30 maximal effects relative to rosiglitazone) and antagonist activity in cell-free and cell-based assays for the PPAR-γ receptor. The compd. is a potent agent for reducing obesity and insulin resistance in fat-fed C57BL/6J mice. This compd. and other PPAR-γ antagonists/partial agonists and pharmaceutically acceptable salts are effective in the treatment of obesity and related disorders, such as diabetes, insulin resistance, hyperlipidemia, atherosclerosis, **inflammation** and cancer.

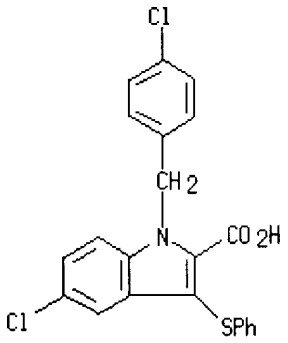
IT **118414-59-8**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(compns. contg. PPAR-γ receptor antagonists/partial agonists for treatment of obesity and related disorders)

RN 118414-59-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 5-chloro-1-[(4-chlorophenyl)methyl]-3-(phenylthio)- (9CI) (CA INDEX NAME)



NO

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:666700 HCAPLUS

DOCUMENT NUMBER: 133:252170

TITLE: Preparation of novel N-cyanomethyl amides as protease inhibitors

INVENTOR(S): Bryant, Clifford M.; Bunin, Barry A.; Kraynack, Erica A.; Patterson, John W.

PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055125	A2	20000921	WO 2000-US6747	20000315
WO 2000055125	A3	20010426		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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EP 1178958	A2	20020213	EP 2000-916343	20000315
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TR 200103390	T2	20020521	TR 2001-20010339	20000315
US 6455502	B1	20020924	US 2000-526090	20000315
TR 200201874	T2	20021021	TR 2002-20020187	20000315
US 6476026	B1	20021105	US 2000-526485	20000315
JP 2002539191	T2	20021119	JP 2000-605556	20000315
EE 200100485	A	20030217	EE 2001-485	20000315
NZ 514234	A	20040227	NZ 2000-514234	20000315
AT 259782	E	20040315	AT 2000-916343	20000315
ZA 2001007494	A	20020911	ZA 2001-7494	20010911
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BG 106003	A	20020628	BG 2001-106003	20011010
HR 2001000738	A1	20021231	HR 2001-738	20011012
US 2002086996	A1	20020704	US 2001-17851	20011214
US 6593327	B2	20030715		
US 2003096796	A1	20030522	US 2002-205600	20020724
US 2003119788	A1	20030626	US 2002-241001	20020909

PRIORITY APPLN. INFO.:

US 1999-124420P	P	19990315
US 2000-526090	A1	20000315
US 2000-526485	A3	20000315
WO 2000-US6747	W	20000315

OTHER SOURCE(S): MARPAT 133:252170
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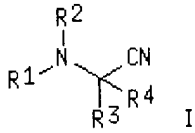

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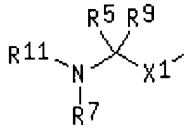
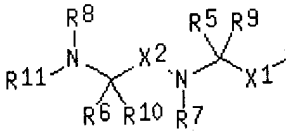


II



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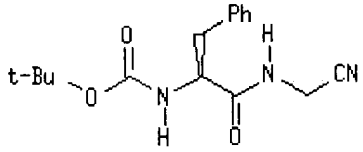


IV

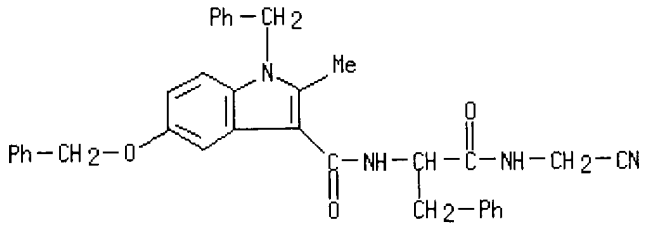
AB The title compds. [I; R1 = II, III (wherein X1, X2 = CO, CH2SO2; R5, R6 = H, alkyl; R7, R8 = H, alkyl, etc.; R9, R10 = alkyl optionally substituted with CN, halo, NO2, etc.; R11 = X5X6R18; X5 = CO, COCO, SO2; X6 = a bond, O, NH, N(alkyl); R18 = alkyl optionally substituted with CN, halo, NO2, etc.); R2 = H, alkyl, etc.; R3 = H, alkyl, etc.; R4 = H, alkyl optionally substituted with CN, halo, NO2, etc.; R4 and R2 taken together form trimethylene, tetramethylene, phenylene-1,2-dimethylene, optionally substituted with hydroxy, oxo or methylene; R4 and R3 together with the carbon atom to which both are attached form cycloalkylene, heterocycloalkylene], useful for treating diseases assocd. with cysteine protease activity, particularly diseases assocd. with activity of cathepsins B, K, L or S such as **inflammation** and asthma, were prepd. and formulated. Thus, reacting 2(S)-tert-butoxycarbonylamino-3-phenylpropionic acid with aminoacetonitrile.HCl in the presence of Et3N in DMF and MeCN afforded the amide (1S)-IV. Biol. data for compds. I were given.

IT **294640-68-9P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of novel N-cyanomethyl amides as protease inhibitors)

RN 294640-68-9 HCAPLUS

CN 1H-Indole-3-carboxamide, N-[2-[(cyanomethyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-2-methyl-5-(phenylmethoxy)-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



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L8 ANSWER 11 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

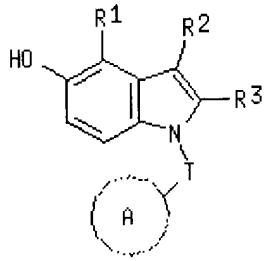
ACCESSION NUMBER:	2000:553553 HCAPLUS
DOCUMENT NUMBER:	133:150460
TITLE:	Preparation of indole derivatives as MCP-1 antagonists
INVENTOR(S):	Faull, Alan Wellington; Kettle, Jason Grant
PATENT ASSIGNEE(S):	Astrazeneca UK Limited, UK
SOURCE:	PCT Int. Appl., 51 pp.
	CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000046196	A1	20000810	WO 2000-GB265	20000131
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356898	AA	20000810	CA 2000-2356898	20000131
BR 2000007984	A	20011106	BR 2000-7984	20000131
EP 1150952	A1	20011107	EP 2000-901259	20000131
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200102233	T2	20011221	TR 2001-200102233	20000131
EE 200100403	A	20021015	EE 2001-403	20000131
JP 2002536359	T2	20021029	JP 2000-597267	20000131
NZ 512680	A	20031128	NZ 2000-512680	20000131
AU 770856	B2	20040304	AU 2000-21213	20000131
ZA 2001005311	A	20020927	ZA 2001-5311	20010627
NO 2001003809	A	20011002	NO 2001-3809	20010803
US 6737435	B1	20040518	US 2001-889599	20011019

PRIORITY APPLN. INFO.: GB 1999-2461 A 19990205
WO 2000-GB265 W 20000131

OTHER SOURCE(S): MARPAT 133:150460
GI



I

ODP = 09/889599
NO = not notified

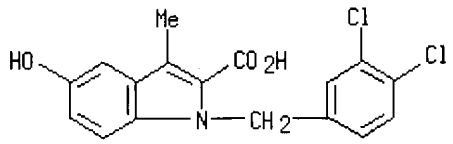
AB The title compds. [I; R1 = H, halo, OMe; R2 = H, halo, Me, Et, OMe; R3 = CO2H, tetrazolyl, CONHSO2R4 (wherein R4 = Me, Et, Ph, 2,5-dimethylisoxazolyl, CF3); T = CH2, SO2; A = 3-ClC6H4, 4-ClC6H4, 2,3-dichloropyrid-5-yl, etc.], useful in the treatment of disease mediated by monocyte chemoattractant protein-1 or RANTES (Regulated Upon Activation, Normal T-cell Expressed and Secreted), such as **inflammatory** disease, were prepd. and formulated. Thus, hydrolysis of Et N-(3,4-dichlorobenzyl)-5-hydroxyindole-2-carboxylate (prepn. given) afforded 89% I [R1, R2 = H; R3 = CO2H; T = CH2; A = 3,4-Cl2C6H3]. Compds. I tested had IC50 of ≤ 50 μM against hMCP-1 receptor binding.

IT **287714-84-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of indole derivs. as MCP-1 antagonists)

RN 287714-84-5 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(3,4-dichlorophenyl)methyl]-5-hydroxy-3-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

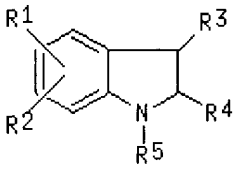
Full Text | Citing References

ACCESSION NUMBER: 1999:566026 HCAPLUS
DOCUMENT NUMBER: 131:199619
TITLE: Preparation of indole derivatives as phospholipase enzyme inhibitors
INVENTOR(S): Seehra, Jasbir S.; Mckew, John C.; Lovering, Frank; Bemis, Jean E.; Xiang, Yibin; Chen, Lihren; Knopf, John L.
PATENT ASSIGNEE(S): Genetics Institute, Inc., USA
SOURCE: PCT Int. Appl., 182 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943654	A2	19990902	WO 1999-US3898	19990224
WO 9943654	A3	19991028		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2322162	AA	19990902	CA 1999-2322162	19990224
AU 9927825	A1	19990915	AU 1999-27825	19990224
AU 765427	B2	20030918		
BR 9908275	A	20001024	BR 1999-8275	19990224
TR 200002447	T2	20001121	TR 2000-200002447	19990224
EP 1062205	A2	20001227	EP 1999-908378	19990224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002504541	T2	20020212	JP 2000-533412	19990224
EE 200000488	A	20020215	EE 2000-488	19990224
NO 2000004219	A	20001023	NO 2000-4219	20000823
HR 2000000551	A1	20010430	HR 2000-551	20000824
BG 104779	A	20011031	BG 2000-104779	20000919

PRIORITY APPLN. INFO.: US 1998-30592 A 19980225
WO 1999-US3898 W 19990224

OTHER SOURCE(S): MARPAT 131:199619
GI



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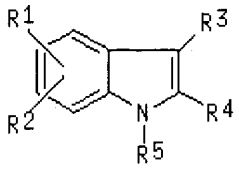

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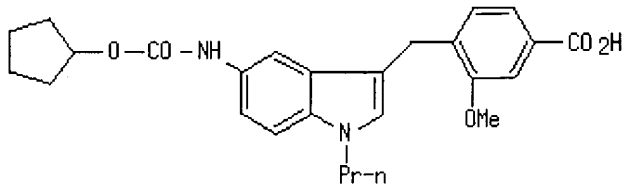
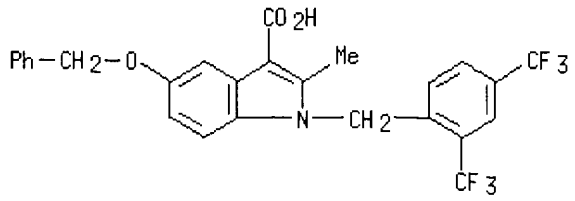


III

AB Indole derivs. (I) and (II) [where R1 = H, halogen, CF3, C1-10 alkyl, S-C1-10 alkyl, C1-10 alkoxy, CN, NO2, NH2, Ph, OPh, SPh, CH2Ph, OCH2Ph, SCH2Ph, or (un)substituted amido, carbamido, sulfonyl, etc.; R2 = H, halogen, CF3, OH, C1-10 alkyl, C1-10 alkoxy, CHO, CN, NO2, (un)substituted amino, SO2-C1-6 alkyl; R3 = (un)substituted carboxylic acid, OPO3H2, SO3H, etc.; R4 = H, CF3, C1-6 alkyl, C1-6 alkoxy, (C1-6 alkyl)cycloalkyl, CHO, halogen, etc.; R5 = C1-6 alkyl, C1-6 alkoxy, (C1-6 alkyl)cycloalkyl, etc.] and pharmaceutically acceptable salts thereof, were prepd. by several methods. Thus, 5-nitroindole was C3-alkylated with Me 4-(bromomethyl)-3-methoxybenzoate in dioxane, N-alkylated with 1-iodopropane in a soln. of THF and NaH, and converted to the amine by hydrogenation over Pt/C. The amine was converted to the carbamate by addn. of cyclopentyl chloroformate in CH2Cl2 and 4-methylmorpholine and the resultant ester hydrolyzed to yield 4-[(5-{[(cyclopentyloxy)carbonyl]amino}-1-propyl-1H-indol-3-yl)methyl]-3-methoxybenzoic acid (III). The title compds. are useful as phospholipase enzyme inhibitors, esp. cytosolic phospholipase A2 (cPLA2), for treatment of **inflammatory** conditions, particularly where inhibition of prodn. of prostaglandins, leukotrienes, and PAF are all desired. Over one hundred compds. of the invention were tested for cPLA2 inhibiting activity in the Coumarine assay and rat carrageenan-induced footpad edema test. Compds. exhibited 7% to 98% inhibition at concns. of 0.125 μM to 400 μM in the Coumarine assay and -7.16% to 34.52% inhibition at concns. of 2 μM to 20 μM in the footpad edema test.

IT **241497-82-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of indole derivs. as phospholipase enzyme inhibitors for treatment of **inflammatory** conditions)

RN 241497-82-5 HCAPLUS
CN 1H-Indole-3-carboxylic acid, 1-[[2,4-bis(trifluoromethyl)phenyl]methyl]-2-methyl-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



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L8 ANSWER 13 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

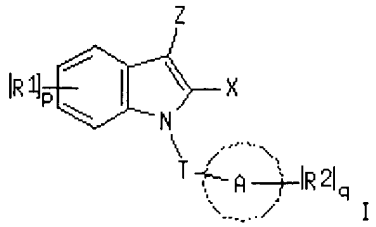
Full Text | Citing References

ACCESSION NUMBER: 1999:126819 HCAPLUS
DOCUMENT NUMBER: 130:182354
TITLE: Preparation of substituted indoles for treatment of a disease or condition mediated by monocyte chemoattractant protein-1 (MCP-1)
INVENTOR(S): Barker, Andrew John; Kettle, Jason Grant; Faull, Alan Wellington
PATENT ASSIGNEE(S): Zeneca Limited, UK
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9907351	A2	19990218	WO 1998-GB2341	19980804
WO 9907351	A3	19990514		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9886381	A1	19990301	AU 1998-86381	19980804
AU 745907	B2	20020411		
EP 1003504	A2	20000531	EP 1998-937659	19980804
EP 1003504	B1	20030702		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
BR 9811818	A	20000815	BR 1998-11818	19980804
TR 200000289	T2	20000821	TR 2000-200000289	19980804
JP 2001513494	T2	20010904	JP 2000-506944	19980804
RU 2217142	C2	20031127	RU 2000-105901	19980804
ZA 9807090	A	19990208	ZA 1998-7090	19980806
HR 2000000061	A1	20001231	HR 2000-61	20000203
US 6441004	B1	20020827	US 2000-485061	20000203
NO 2000000573	A	20000204	NO 2000-573	20000204
HK 1027979	A1	20031031	HK 2000-107435	20001121
US 2003119830	A1	20030626	US 2002-194969	20020715

PRIORITY APPLN. INFO.:
GB 1997-16657 A 19970807
WO 1998-GB2341 W 19980804
US 2000-485061 A1 20000203

OTHER SOURCE(S): MARPAT 130:182354
GI



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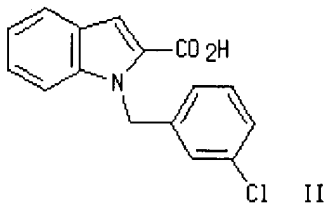


II

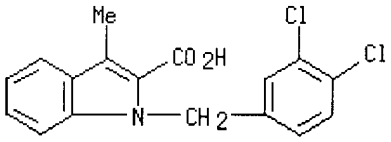
AB The title compds. [I; R1 = CF3, alkyl, halo, etc.; p = 0-4; T = (CHR4)m (wherein R4 = H, alkyl; m = 1-3); X = CO2R4, SO3H, CN, etc.; A = Ph, naphthyl, furyl, etc.; R2 = CF3, alkyl, halo, etc.; q = 0-4; Z = H, halo, Me, etc.] and their pharmaceutically acceptable salts or in vivo hydrolysable esters, useful in the treatment of a disease or condition mediated by monocyte chemoattractant protein-1 (MCP-1) such as rheumatoid arthritis, asthma, atherosclerosis, psoriasis, **inflammatory** bowel disease and stroke, were prepd. and formulated. Thus, hydrolysis of Et N-(3-chlorobenzyl)indole-2-carboxylate with 2N NaOH in THF/MeOH afforded 82% II. The tested compds. I showed generally IC50 of < 50 μM in the hMCP-1 receptor binding assay.

IT **220678-49-9P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted indoles for treatment of a disease or condition mediated by monocyte chemoattractant protein-1 (MCP-1))

RN 220678-49-9 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(3,4-dichlorophenyl)methyl]-3-methyl- (9CI) (CA INDEX NAME)



L8 ANSWER 14 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1995:638471 HCAPLUS
DOCUMENT NUMBER: 123:32958
TITLE: Indole-2-alkanoic acids and their derivatives as inhibitors of phospholipase A2.
INVENTOR(S): Lehr, Matthias
PATENT ASSIGNEE(S): Germany
SOURCE: Ger. Offen., 30 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

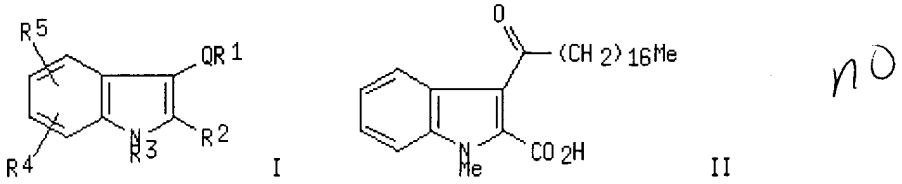
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4338770	A1	19950518	DE 1993-4338770	19931112
WO 9513266	A1	19950518	WO 1994-DE1121	19940920

W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK,

TJ, TT, UA, US, UZ, VN
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9476907 A1 19950529 AU 1994-76907 19940920
PRIORITY APPLN. INFO.: DE 1993-4338770 19931112
WO 1994-DE1121 19940920

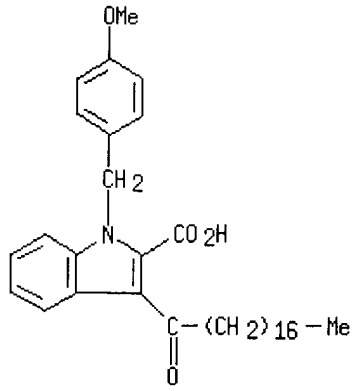
OTHER SOURCE(S): MARPAT 123:32958
GI



AB Title compds. I [R1 = X, (un)substituted aryl, -X-aryl; X = C1-19 alk(en/yn)yl optionally interrupted by O; R2 = CO2H, -Y-CO2H, Tz, -Y-Tz; Y = C1-8 alk(en)yl optionally interrupted by O; Tz = 1H- or 2H-tetrazol-5-yl; R3 = H, Z (Z = C1-20 alk(en/yn)yl optionally interrupted by O), (un)substituted aryl or -Z-aryl, or Z (un)substituted by OH, acyloxy, SH, acylthio, NH2, or acylamino; Q = CO, CH2, (acylamino)methylene; R4, R5 = H, as given for Z, halo, CF3, OH, cyano, many others] and their pharmaceutical salts and esters are claimed. The compds. are inhibitors of phospholipase A2 (PLA2), and are claimed useful for treatment or prevention of **inflammation**, allergy, asthma, psoriasis, and endotoxin shock. For example, acylation of indole-2-carboxylic acid Et ester with octadecanoic acid in CH2Cl2 in the presence of polyphosphoric acid and (CF3CO)2O gave 42% 3-octadecanoyl deriv., which was N-alkylated by p-MeC6H4SO3Me under phase-transfer conditions (75%) and hydrolyzed by aq. KOH in refluxing EtOH (80%) to give title compd. II. In a test for inhibition of PLA2 using bovine platelets in vitro, II at 10 μM gave 61% inhibition, vs. only 42% for the known inhibitor (S)-N-hexadecyl-2-pyrrolidinecarboxamide.

IT **164160-85-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of indolealkanoic acids as phospholipase A2 inhibitors)

RN 164160-85-4 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(4-methoxyphenyl)methyl]-3-(1-oxooctadecyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 15 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

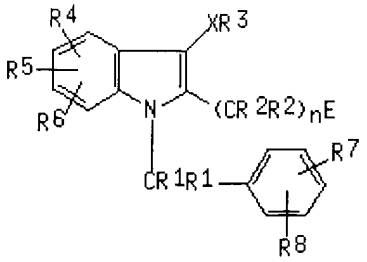
Full Text | Citing References

ACCESSION NUMBER: 1992:255478 HCAPLUS
DOCUMENT NUMBER: 116:255478
TITLE: Preparation of 3-alkylthio-N-benzylindoles and related compounds as leukotriene inhibitors
INVENTOR(S): Gillard, John W.; Morton, Howard E.; Fortin, Rejean; Guindon, Yvan
PATENT ASSIGNEE(S): Merck Frosst Canada Inc., Can.
SOURCE: U.S., 30 pp. Cont.-in-part of U.S. Ser. No. 942,900, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5081138	A	19920114	US 1987-130771	19871209
CA 1334415	A1	19950214	CA 1987-553922	19871209
US 5225421	A	19930706	US 1991-760443	19910916

PRIORITY APPLN. INFO.: US 1986-942900 19861217
US 1987-130771 19871209

OTHER SOURCE(S): MARPAT 116:255478
GI



I

AB Title compds. I [R1, R2 = H, C1-7 alkyl; CR2R2 = 3-6 membered ring; R3 = (substituted) C1-20 alkyl, C2-6 alkenyl, (substituted) Ph, (CH2)mHet; R4-R6 = H, C1-7 alkyl, C2-6 alkenyl, (CR2R2)pM; R7, R8 = H, C1-3 alkyl, halo, OH, cyano, CF3, C1-3 alkoxy, C1-3 alkylthio, CO2H, C1-3 alkoxycarbonyl, C1-3 alkylcarbonyl, N3; R9 = CF3, C1-7 alkyl, (substituted) benzyl, (substituted) Ph; R10 = H, C1-7 alkyl, Ph, CH2Ph; NR10R10 = 5-7 membered ring; R11 = H, (CH2)qR9; R13 = H, C1-7 alkyl,

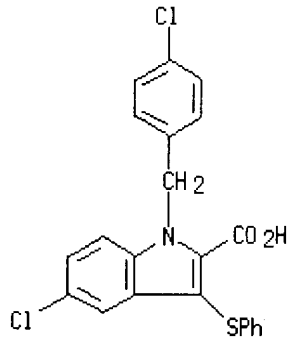
(substituted) Ph, (substituted) benzyl; R14 = CH2CH2N(R10)2, CH2CHOHCH2OH, CH2O2CCMe3, CHMeO2CCMe, etc.; E = CH2OH, CO2R13, CO2R14, tetrazol-5-yl, CHO, CONR2R2, CONHSO2R9, CON(OR2)R2; M = OR10, halo, CF3, SR7, (substituted) Ph, CO2R10, COR11, tetrazolyl, etc.; X = O, S, SO, SO2, Het = pyridyl, tetrazolyl, thienyl, thiazolyl, etc.; m = 0-2; n = 0-5; p = 0-3; q = 0-4] were prepd. as leukotriene inhibitors useful as antiasthmatics, antiallergics, antiinflammatories, and cytoprotective agents (no data). Thus, 1-p-chlorobenzyl-1-(4-fluorophenyl)hydrazine.HCl was added to Et 4-methylthio-3-oxobutanoate in Me3COH and the mixt. was refluxed under N for 16 h to give title compd. I [R1, R2, R5-R7 = H; R3 = Me; R4 = 5-F; R8 = 4-Cl; n = 1; E = CO2Et; X = S].

IT **118414-59-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as leukotriene inhibitor)

RN 118414-59-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 5-chloro-1-[(4-chlorophenyl)methyl]-3-(phenylthio)- (9CI) (CA INDEX NAME)



L8 ANSWER 16 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

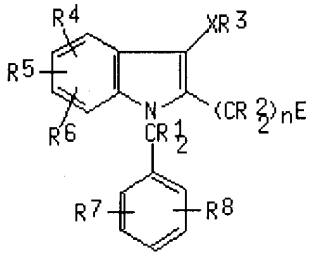
Full Text | Citing References

ACCESSION NUMBER: 1989:57508 HCAPLUS
DOCUMENT NUMBER: 110:57508
TITLE: Preparation and formulation of 3-hetero-substituted-N-benzyl-indoles as inhibitors of leukotriene biosynthesis
INVENTOR(S): Gillard, John W.; Morton, Howard E.; Fortin, Rejean; Guindon, Yvan
PATENT ASSIGNEE(S): Merck Frosst Canada, Inc., Can.
SOURCE: Eur. Pat. Appl., 78 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 275667	A1	19880727	EP 1987-311031	19871215
EP 275667	B1	19920318		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
IL 84796	A1	19920329	IL 1987-84796	19871211
ZA 8709401	A	19880727	ZA 1987-9401	19871215
AT 73770	E	19920415	AT 1987-311031	19871215

AU 8782603	A1	19880623	AU 1987-82603	19871216
AU 603402	B2	19901115		
DK 8706608	A	19880925	DK 1987-6608	19871216
JP 63246372	A2	19881013	JP 1987-317663	19871217
PRIORITY APPLN. INFO.:			CA 1986-525670	19861217
			EP 1987-311031	19871215

OTHER SOURCE(S): MARPAT 110:57508
GI

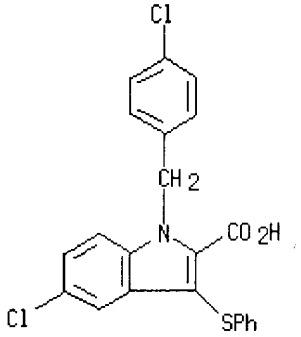


I

AB Title compds. I [R1 = H, alkyl; R2 = H, alkyl, R22 = C3-6 ring; R3 = alkyl, C3-6 alkenyl, (un)substituted Ph, R(CH2)m, M-substituted alkyl; R = heterocyclyl; m = 0-2; M = halo, F3C, F3CS, (un)substituted Ph, tetrazole, O2N, H, etc.; R4, R5, R6 = H, alkyl; C2-6 alkenyl, etc; R7, R8 = H, C1-3 alkyl, halo, HO, cyano, F3C, C1-3 alkoxy, C1-3 alkylthio, HO2C, C1-3 alkoxycarbonyl, C1-3 alkylcarbonyl, N3; E = HOCH2, HO2C, alkyl-O2C, (un) substituted PhO2C, tetrazol-5-yl, HCO, HOCH2CH(OH)CH2O2C, etc.; X = O, S, SO, SO2; n = 0-5] and their pharmaceutically acceptable salts, useful as inhibitors of leukotriene biosynthesis (no data), were prepd. To Et 5-chloro-3-(phenylthio)indole-2-carboxylate in THF was added K hexamethylsilamide in PhMe, followed by 4-ClC6H4CH2Cl, Hempa and Bu4NBr to give I (R1, R5, R6, R8 = H; R3 = Ph; R4 = 5-Cl; R1 = 4-Cl; n = 0; E = EtO2C).

IT **118414-59-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as leukotriene biosynthesis inhibitor)

RN 118414-59-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 5-chloro-1-[(4-chlorophenyl)methyl]-3-(phenylthio)- (9CI) (CA INDEX NAME)



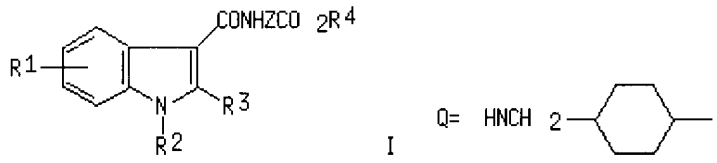
L8 ANSWER 17 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1988:94380 HCAPLUS
DOCUMENT NUMBER: 108:94380
TITLE: Preparation of 3-indolecarboxamide derivatives as analgesics, **inflammation** inhibitors and 5-lipoxygenase inhibitors
INVENTOR(S): Nakao, Tatsu; Saito, Tadamasa; Terasawa, Michio; Tawara, Tetsuji
PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 62138469	A2	19870622	JP 1985-278472	19851211

PRIORITY APPLN. INFO.: JP 1985-278472 19851211
GI

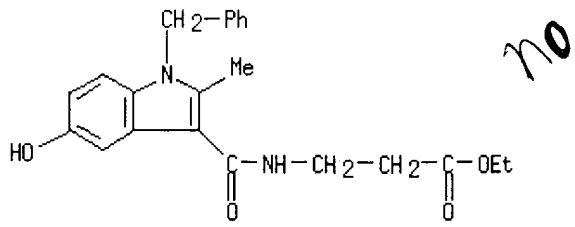


I

AB The title compds. [I; R1 = H, halo, OH, alkanoyl; R2 = H, alkyl, (substituted) Ph, aralkyl; R3 = alkyl; R4 = H, alkyl; Z = C1-6 alkylene, cyclohexylenemethyl, phenylene], useful as analgesics, antiinflammatory agents, and 5-lipoxygenase inhibitors, are prepd. Treatment of 5-hydroxy-2-methylindole-3-carboxylic acid and Et trans-4-aminoethylcyclohexane-1-carboxylate.HCl in THF with 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide in the presence of Et3N gave I (R1 = 5-OH; R2 = H; R3 = Me; R4 = Et; Z = trans-Q). I (R1 = 5-OH; R2 = PhCH2; R3 = Me; R4 = Et; Z = trans-Q) at 100 mg/kg p.o. showed 62% analgesic activity in rats treated with phenylquinone i.p.

IT **113077-88-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as analgesic, antiinflammatory agent, and lipoxygenase inhibitor)

RN 113077-88-6 HCAPLUS
CN β-Alanine, N-[[5-hydroxy-2-methyl-1-(phenylmethyl)-1H-indol-3-yl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)



L8 ANSWER 18 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

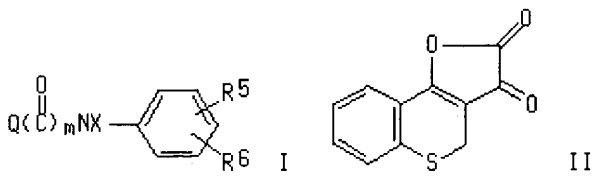
ACCESSION NUMBER: 1988:21703 HCAPLUS
DOCUMENT NUMBER: 108:21703
TITLE: Preparation of heterocyclic enol amide derivatives as pharmaceuticals
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 78 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 62081369	A2	19870414	JP 1986-230231	19860930
US 4761424	A	19880802	US 1985-782623	19851001
ZA 8606973	A	19880427	ZA 1986-6973	19860912
AU 8663285	A1	19870402	AU 1986-63285	19860929
AU 605747	B2	19910124		
DK 8604664	A	19870406	DK 1986-4664	19860930
EP 221345	A1	19870513	EP 1986-113489	19861001
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ES 2002398	A6	19880801	ES 1986-2338	19861001
US 4921871	A	19900501	US 1987-121264	19871116
US 4874758	A	19891017	US 1988-164355	19880304
US 4868195	A	19890919	US 1988-165045	19880307
US 4868199	A	19890919	US 1988-167264	19880309
US 4868200	A	19890919	US 1988-166146	19880309
US 4868205	A	19890919	US 1988-167272	19880311

PRIORITY APPLN. INFO.: US 1985-782623 19851001
US 1987-121264 19871116

OTHER SOURCE(S): CASREACT 108:21703

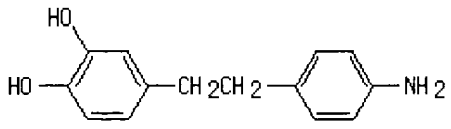
GI



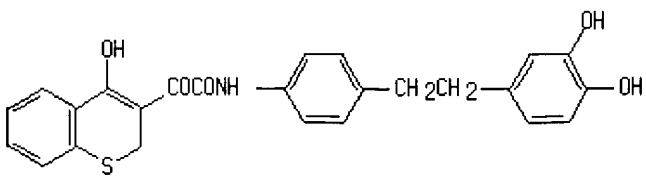
I

II

no



III



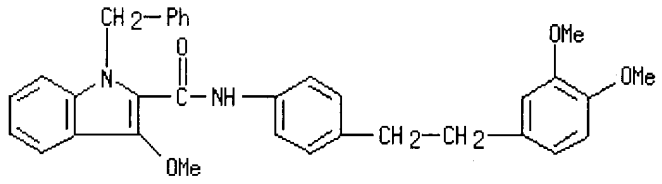
IV

AB The title compds. (I; Q = benzofuryl, benzothienyl, indolyl, benzopyranyl, benzothiopyranyl, etc.; R5 = H, C1-4 alkyl, alkoxy, C2-4 carbalkoxy, etc.; R6 = C6-20 alkyl, styryl, etc.; X = H, alkyl; m = 1, 2), useful as pharmaceuticals, are prepd. A mixt. of 0.085 mol furandione deriv. II and 0.0749 mol aniline deriv. III in THF was stirred at room temp. under N, the solvent distd. in vacuo, and the solid product was refluxed in CH2Cl2 to give 85.2% enol amide IV. I showed ID50 against 5-lipoxygenase at 1.06-9.30M.

IT **111926-88-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as drug)

RN 111926-88-6 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[4-[2-(3,4-dimethoxyphenyl)ethyl]phenyl]-3-methoxy-1-(phenylmethyl)- (9CI) (CA INDEX NAME)

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     FILE 'REGISTRY' ENTERED AT 14:50:49 ON 15 JUN 2004
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L2               0 S L1
L3             514 S L1 FULL
L4             STRUCTURE UPLOADED
L5               0 S L4
L6               0 S L4 FULL

     FILE 'HCAPLUS' ENTERED AT 15:02:52 ON 15 JUN 2004
L7              37 S L3/THU
L8              18 S L7 AND INFLAMM?

=> s l8 and faull, a?/au
            34 FAULL, A?/AU
L9               3 L8 AND FAULL, A?/AU

=> s l7 and faull, a?/au
            34 FAULL, A?/AU
L10              4 L7 AND FAULL, A?/AU

=> d l10, ibib abs fhitstr, 1-4

L10  ANSWER 1 OF 4  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

ACCESSION NUMBER: 2001:526057 HCAPLUS
DOCUMENT NUMBER: 135:107248
TITLE: Preparation of indole-2-carboxylic acids as MCP-1 receptor antagonists

INVENTOR(S): **Faull, Alan Wellington**; Kettle, Jason Grant
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001051466	A1	20010719	WO 2001-GB69	20010111
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2001007404	A	20021008	BR 2001-7404	20010111
EP 1252142	A1	20021030	EP 2001-900494	20010111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003519683	T2	20030624	JP 2001-551848	20010111
EE 200200394	A	20031215	EE 2002-394	20010111
BG 106894	A	20030430	BG 2002-106894	20020702
US 2003144339	A1	20030731	US 2002-169717	20020709
NO 2002003380	A	20020903	NO 2002-3380	20020712

PRIORITY APPLN. INFO.: GB 2000-626 A 20000113
WO 2001-GB69 W 20010111

OTHER SOURCE(S): MARPAT 135:107248
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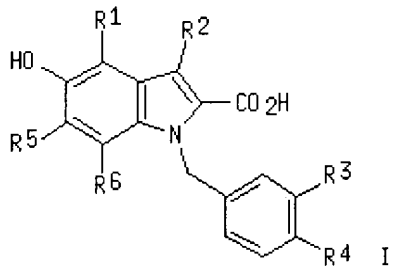
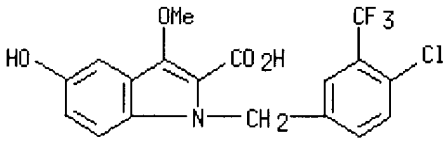


I

10/169717 OPP

AB The title compds. [I; R1 = H, halo, OMe; R2 = H, halo, Me, Et, OMe; R3 = halo, CF3; R4 = halo, CF3; R5 = H, halo; R6 = H, halo; provided that when R5 and R6 are both H atom, and one of R3 or R4 is Cl or F, then the other is not Cl or F] and their prodrugs which have useful activity for the treatment of inflammatory disease, specifically in antagonizing an MCP-1 mediated effect in a warm-blooded animal such as a human being, were prepd. and formulated. Thus, reacting Et N-(3-trifluoromethyl 4-chlorobenzyl)-5-acetoxyindole-2-carboxylate (prepn. given) with NaOH in H2O/MeOH followed by treatment with 2M HCl afforded 71% I [R1, R2, R5, R6 = H; R3 = CF3; R4 = Cl]. The tested compds. I had IC50's of ≤ 50 μM in the hMCP-1 receptor binding assay.

IT **350596-52-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of indole-2-carboxylic acids as MCP-1 receptor antagonists)
RN 350596-52-0 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[[4-chloro-3-(trifluoromethyl)phenyl]methyl]-5-hydroxy-3-methoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:553556 HCAPLUS
DOCUMENT NUMBER: 133:150463
TITLE: Preparation of 3-substituted indole-2-carboxylic acids for the inhibition of monocyte chemoattractant protein-1 and/or RANTES induced chemotaxis
INVENTOR(S): **Faull, Alan Wellington**; Kettle, Jason
PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000046199	A2	20000810	WO 2000-GB284	20000131
WO 2000046199	A3	20001130		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2355734	AA	20000810	CA 2000-2355734	20000131
BR 2000008015	A	20011106	BR 2000-8015	20000131
EP 1173421	A2	20020123	EP 2000-901747	20000131
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002536362	T2	20021029	JP 2000-597270	20000131
ZA 2001005017	A	20020919	ZA 2001-5017	20010619
NO 2001003768	A	20011001	NO 2001-3768	20010801

PRIORITY APPLN. INFO.: GB 1999-2455 A 19990205
WO 2000-GB284 W 20000131
OTHER SOURCE(S): MARPAT 133:150463
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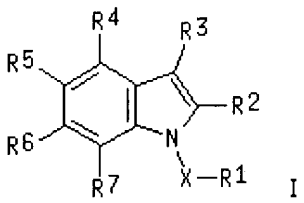

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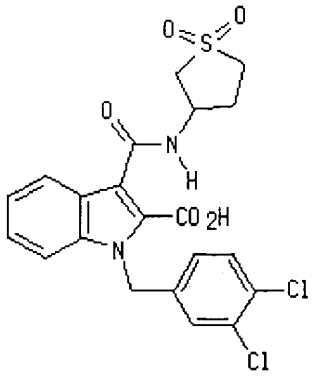


II

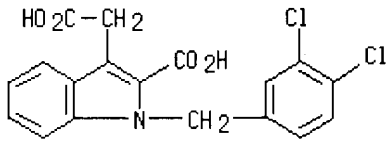
AB The title compds. [I; X = CH2, SO2; R1 = (un)substituted aryl, heteroaryl; R2 = CO2H, CN, COCH2OH, etc.; R3 = OR15 (wherein R15 = substituted alkyl or cycloalkyl, (un)substituted heteroaryl), S(O)qR15 (q = 0-2), (CH2)sCO2H (s = 0-4), etc.; R4-R7 = H, (un)substituted hydrocarbyl, heterocyclyl, etc.] and their pharmaceutically acceptable salts, amides or esters, useful in the prepn. of a medicament for the inhibition of monocyte chemoattractant protein-1 and/or RANTES induced chemotaxis, were prepd. and formulated. Thus, hydrolysis of the corresponding ester afforded 93% II which showed IC50 of 6.86 μM against hMCP-1 receptor binding.

IT **287725-35-3P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of 3-substituted indole-2-carboxylic acids for the inhibition of monocyte chemoattractant protein-1 and/or RANTES induced chemotaxis)

RN 287725-35-3 HCAPLUS

CN 1H-Indole-3-acetic acid, 2-carboxy-1-[(3,4-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:553553 HCAPLUS
DOCUMENT NUMBER: 133:150460
TITLE: Preparation of indole derivatives as MCP-1 antagonists
INVENTOR(S): **Faull, Alan Wellington**; Kettle, Jason Grant
PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000046196	A1	20000810	WO 2000-GB265	20000131
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356898	AA	20000810	CA 2000-2356898	20000131
BR 2000007984	A	20011106	BR 2000-7984	20000131
EP 1150952	A1	20011107	EP 2000-901259	20000131
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200102233	T2	20011221	TR 2001-200102233	20000131
EE 200100403	A	20021015	EE 2001-403	20000131
JP 2002536359	T2	20021029	JP 2000-597267	20000131
NZ 512680	A	20031128	NZ 2000-512680	20000131
AU 770856	B2	20040304	AU 2000-21213	20000131
ZA 2001005311	A	20020927	ZA 2001-5311	20010627
NO 2001003809	A	20011002	NO 2001-3809	20010803
US 6737435	B1	20040518	US 2001-889599	20011019

PRIORITY APPLN. INFO.: GB 1999-2461 A 19990205
WO 2000-GB265 W 20000131

OTHER SOURCE(S): MARPAT 133:150460

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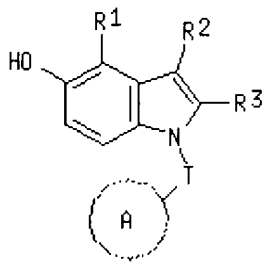


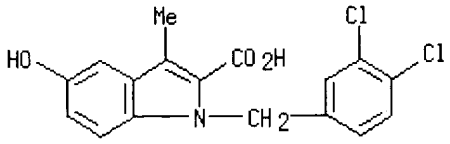
I

AB The title compds. [I; R1 = H, halo, OMe; R2 = H, halo, Me, Et, OMe; R3 = CO2H, tetrazolyl, CONHSO2R4 (wherein R4 = Me, Et, Ph, 2,5-dimethylisoxazolyl, CF3); T = CH2, SO2; A = 3-ClC6H4, 4-ClC6H4, 2,3-dichloropyrid-5-yl, etc.], useful in the treatment of disease mediated by monocyte chemoattractant protein-1 or RANTES (Regulated Upon Activation, Normal T-cell Expressed and Secreted), such as inflammatory disease, were prepd. and formulated. Thus, hydrolysis of Et N-(3,4-dichlorobenzyl)-5-hydroxyindole-2-carboxylate (prepn. given) afforded 89% I [R1, R2 = H; R3 = CO2H; T = CH2; A = 3,4-Cl2C6H3]. Compds. I tested had IC50 of ≤ 50 μM against hMCP-1 receptor binding.

IT **287714-84-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of indole derivs. as MCP-1 antagonists)

RN 287714-84-5 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(3,4-dichlorophenyl)methyl]-5-hydroxy-3-

methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:126819 HCAPLUS
DOCUMENT NUMBER: 130:182354
TITLE: Preparation of substituted indoles for treatment of a disease or condition mediated by monocyte chemoattractant protein-1 (MCP-1)
INVENTOR(S): Barker, Andrew John; Kettle, Jason Grant; **Faull, Alan Wellington**
PATENT ASSIGNEE(S): Zeneca Limited, UK
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9907351	A2	19990218	WO 1998-GB2341	19980804
WO 9907351	A3	19990514		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9886381	A1	19990301	AU 1998-86381	19980804
AU 745907	B2	20020411		
EP 1003504	A2	20000531	EP 1998-937659	19980804
EP 1003504	B1	20030702		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
BR 9811818	A	20000815	BR 1998-11818	19980804
TR 200000289	T2	20000821	TR 2000-200000289	19980804
JP 2001513494	T2	20010904	JP 2000-506944	19980804
RU 2217142	C2	20031127	RU 2000-105901	19980804
ZA 9807090	A	19990208	ZA 1998-7090	19980806
HR 2000000061	A1	20001231	HR 2000-61	20000203
US 6441004	B1	20020827	US 2000-485061	20000203
NO 2000000573	A	20000204	NO 2000-573	20000204
HK 1027979	A1	20031031	HK 2000-107435	20001121
US 2003119830	A1	20030626	US 2002-194969	20020715

PRIORITY APPLN. INFO.: GB 1997-16657 A 19970807
WO 1998-GB2341 W 19980804
US 2000-485061 A1 20000203

10/194969

No = Diff at Z2

OTHER SOURCE(S): MARPAT 130:182354
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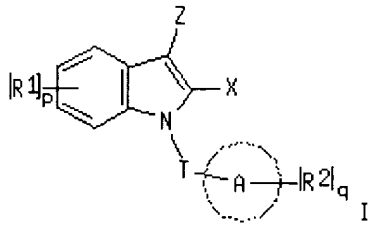

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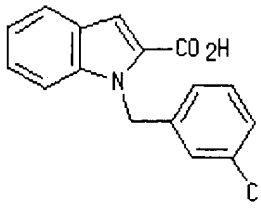
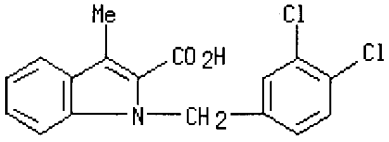


II

AB The title compds. [I; R1 = CF3, alkyl, halo, etc.; p = 0-4; T = (CHR4)m (wherein R4 = H, alkyl; m = 1-3); X = CO2R4, SO3H, CN, etc.; A = Ph, naphthyl, furyl, etc.; R2 = CF3, alkyl, halo, etc.; q = 0-4; Z = H, halo, Me, etc.] and their pharmaceutically acceptable salts or in vivo hydrolysable esters, useful in the treatment of a disease or condition mediated by monocyte chemoattractant protein-1 (MCP-1) such as rheumatoid arthritis, asthma, atherosclerosis, psoriasis, inflammatory bowel disease and stroke, were prepd. and formulated. Thus, hydrolysis of Et N-(3-chlorobenzyl)indole-2-carboxylate with 2N NaOH in THF/MeOH afforded 82% II. The tested compds. I showed generally IC50 of < 50 μM in the hMCP-1 receptor binding assay.

IT **220678-49-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted indoles for treatment of a disease or condition mediated by monocyte chemoattractant protein-1 (MCP-1))

RN 220678-49-9 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(3,4-dichlorophenyl)methyl]-3-methyl- (9CI) (CA INDEX NAME)



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FILE 'REGISTRY' ENTERED AT 14:50:49 ON 15 JUN 2004
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L2 0 S L1
L3 514 S L1 FULL
L4 STRUCTURE UPLOADED
L5 0 S L4
L6 0 S L4 FULL

FILE 'HCAPLUS' ENTERED AT 15:02:52 ON 15 JUN 2004
L7 37 S L3/THU
L8 18 S L7 AND INFLAMM?
L9 3 S L8 AND FAULL, A?/AU
L10 4 S L7 AND FAULL, A?/AU

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L13          0 L12 NOT L10

=> s l7 not l12
L14         33 L7 NOT L12

=> d l14, ibib abs fhitstr, 1-33

L14  ANSWER 1 OF 33  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

ACCESSION NUMBER: 2003:1006815 HCAPLUS
DOCUMENT NUMBER: 140:35974
TITLE: Treatment for depression and anxiety by the combination of a PDE IV inhibitor and an antidepressant or an anxiolytic agent
INVENTOR(S): Sobolov-Jaynes, Susan Beth; Schmidt, Christopher Joseph
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

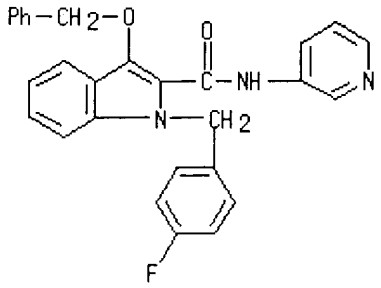
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003105902	A1	20031224	WO 2003-IB2295	20030605
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003235631	A1	20031225	US 2003-387060	20030312

PRIORITY APPLN. INFO.: US 2002-389181P P 20020617
OTHER SOURCE(S): MARPAT 140:35974

AB The present invention relates to a method of treating depression or anxiety in a mammal, including a human, by administering to the mammal a PDE IV inhibitor in combination with an antidepressant or an anxiolytic agent. It also relates to pharmaceutical compns. contg. a pharmaceutically acceptable carrier, a PDE IV inhibitor and an anxiolytic agent or antidepressant.

IT **359001-45-9**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(treatment for depression and anxiety by combination of a PDE IV

inhibitor and an antidepressant or an anxiolytic agent)
RN 359001-45-9 HCAPLUS
CN 1H-Indole-2-carboxamide, 1-[(4-fluorophenyl)methyl]-3-(phenylmethoxy)-N-3-pyridinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:551494 HCAPLUS
DOCUMENT NUMBER: 139:101027
TITLE: Preparation of mercaptoethyl indolecarboxylic acids as NAALAdase inhibitors for treating and diagnosing glutamate abnormalities, neurological and other disorders
INVENTOR(S): Tsukamoto, Takashi; Grella, Brian; Majer, Pavel
PATENT ASSIGNEE(S): Guilford Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

nd

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057670	A2	20030717	WO 2002-US37617	20021219
WO 2003057670	A3	20031106		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-342764P P 20011228
OTHER SOURCE(S): MARPAT 139:101027
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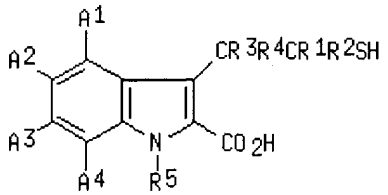


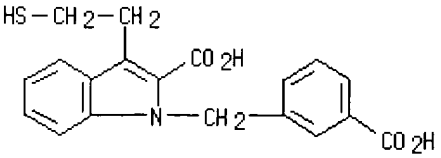
I

AB This invention relates to new indoles (shown as I; variables defined below; e.g. 3-(2-mercaptoethyl)-1H-indole-2-carboxylic acid), pharmaceutical compns. and diagnostic kits comprising such compds., and methods of using such compds. for inhibiting NAALADase enzyme activity, detecting diseases where NAALAdase levels are altered, affecting neuronal activity, effecting TGF-β activity, inhibiting angiogenesis, and treating glutamate abnormalities, neuropathy, pain, compulsive disorders, prostate diseases, cancers and glaucoma. IC50 values are tabulated for inhibition of NAALAdase by 12 examples of I. Many pharmacol. and therapeutic test results are reported for the following 6 compds. that are not covered by I: 2-[[(2,3,4,5,6-pentafluorobenzyl)hydroxyphosphinyl]methyl]pentanedioic acid, 2-(3-sulfanylpropyl)pentanedioic acid, 2-(phosphonomethyl)pentanedioic acid, 2-(2-sulfanylethyl)pentanedioic acid, 3-carboxy-α-(3-mercaptopropyl)benzenepropanoic acid and 3-carboxy-5-(1,1-dimethylethyl)-α-(3-mercaptopropyl)benzenepropanoic acid. For I: A1, A2, A3 and A4 = H, C1-C9 alkyl, C2-C9 alkenyl, C2-C9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, C1-C9 alkoxy, C2-C9 alkenyloxy, phenoxy, benzyloxy, hydroxy, halo, nitro, cyano, isocyano, -COOR6, - COR6, -NR6R7, -SR6, -SOR6, -SO2R6, -SO2(OR6), -C(O)NR6R7, -C(O)NR6 (CH2)nCOOH, -NR6C(O)R7 or -(CH2)nCOOH, or any adjacent two of A1, A2, A3 and A4 form with the benzene ring a fused ring that is (un)satd., arom. or nonarom., and carbocyclic or heterocyclic, said heterocyclic ring contg. 1 or 2 O, N and/or S heteroatom(s); n is 1-3; R, R1, R2, R3, R4, R5, R6, R7 = H, carboxy, C1-C9 alkyl, C2-C9 alkenyl, C2-C9 alkynyl, aryl, heteroaryl, carbocycle or heterocycle; and said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenyloxy, phenoxy, benzyloxy and fused ring (un)substituted with ≥1 substituent(s). Although the methods of prepn. are not claimed, 13 example prepns. are included.

IT **560131-44-4P**, 1-[(3-Carboxyphenyl)methyl]-3-(2-mercaptoethyl)-1H-indole-2-carboxylic acid
RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate and diagnosis agent; prepn. of mercaptoethyl indolecarboxylic acids as NAALAdase inhibitors for treating and diagnosing glutamate abnormalities and neurol. and other disorders)

RN 560131-44-4 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(3-carboxyphenyl)methyl]-3-(2-mercaptoethyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 3 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

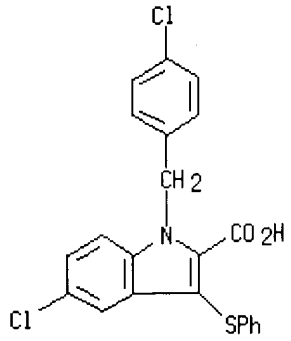
Full Text | Citing References

ACCESSION NUMBER: 2003:294703 HCAPLUS
DOCUMENT NUMBER: 139:143707
TITLE: Distinct properties and advantages of a novel peroxisome proliferator-activated protein γ selective modulator
AUTHOR(S): Berger, Joel P.; Petro, Ann E.; Macnaul, Karen L.; Kelly, Linda J.; Zhang, Bei B.; Richards, Karen; Elbrecht, Alex; Johnson, Bruce A.; Zhou, Gaochao; Doebber, Thomas W.; Biswas, Chhabi; Parikh, Mona; Sharma, Neelam; Tanen, Michael R.; Thompson, G. Marie; Ventre, John; Adams, Alan D.; Mosley, Ralph; Surwit, Richard S.; Moller, David E.
CORPORATE SOURCE: Department of Metabolic Disorders, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Molecular Endocrinology (2003), 17(4), 662-676
CODEN: MOENEN; ISSN: 0888-8809
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Antidiabetic thiazolidinediones (TZDs) and non-TZD compds. have been shown to serve as agonists of the peroxisome proliferator-activated receptor γ (PPARγ). Here, we report the identification and characterization of a novel non-TZD selective PPARγ modulator (nTZDpa). NTZDpa bound potently to PPARγ with high selectivity vs. PPARα or PPARδ. In cell-based assays for transcriptional activation, nTZDpa served as a selective, potent PPARγ partial agonist and was able to antagonize the activity of PPARγ full agonists. NTZDpa also displayed partial agonist effects when its ability to promote adipogenesis in 3T3-L1 cells was evaluated. Assessment of protein conformation using protease protection or soln. NMR spectroscopy methods showed that nTZDpa produced altered PPARγ conformational stability vs. full agonists, thereby establishing a phys. basis for its obsd. partial agonism. DNA microarray anal. of RNA from 3T3-L1 adipocytes treated with nTZDpa or several structurally diverse PPARγ full agonists demonstrated qual. differences in the affected gene expression profile for nTZDpa. Chronic treatment of fat-fed, C57BL/6J mice with nTZDpa or a TZD full agonist ameliorated hyperglycemia and hyperinsulinemia. However, unlike the TZD, nTZDpa caused redns. in wt. gain and adipose depot size. Feed efficiency was also substantially diminished. Unlike TZDs, nTZDpa did not cause cardiac hypertrophy in mice. When a panel of PPARγ target genes was examd. in white adipose tissue, nTZDpa produced a different in vivo expression pattern vs. the full agonist. These findings establish that novel selective PPARγ modulators can produce altered receptor conformational stability leading to distinctive gene expression profiles, reduced adipogenic cellular effects, and potentially improved in vivo biol. responses. Such compds. may lead to preferred therapies for diabetes, obesity, or metabolic syndrome.

IT **118414-59-8**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(novel PPARγ partial agonist in relation to PPARγ conformation, adipocyte gene expression, and potential treatment of diabetes, obesity, or metabolic syndrome)

RN 118414-59-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 5-chloro-1-[(4-chlorophenyl)methyl]-3-(phenylthio)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

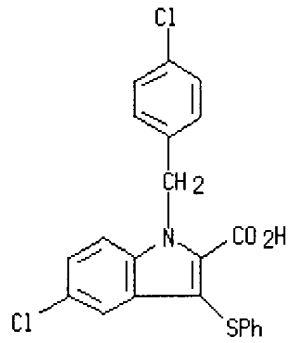
ACCESSION NUMBER: 2003:273638 HCAPLUS
DOCUMENT NUMBER: 139:207415
TITLE: A non-thiazolidinedione partial peroxisome proliferator-activated receptor γ ligand inhibits vascular smooth muscle cell growth
AUTHOR(S): Bruemmer, Dennis; Berger, Joel P.; Liu, Joey; Kintscher, Ulrich; Wakino, Shu; Fleck, Eckart; Moller, David E.; Law, Ronald E.
CORPORATE SOURCE: David Geffen School of Medicine, Diabetes and Hypertension and The Gonda (Goldschmied) Diabetes Center, Division of Endocrinology, University of California, Los Angeles, CA, 90095-7073, USA
SOURCE: European Journal of Pharmacology (2003), 466(3), 225-234
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several peroxisome proliferator-activated receptor γ (PPARγ) agonists of the thiazolidinedione class inhibit vascular smooth muscle cell proliferation. It is not known whether the antiproliferative activity of PPARγ agonists is limited to the thiazolidinedione class and/or is directly mediated through PPARγ-dependent transactivation of target genes. We report here that a novel non-thiazolidinedione partial PPARγ agonist (nTZDpa) attenuates rat aortic vascular smooth muscle cell proliferation. In a transfection assay for PPARγ transcriptional activation, the non-thiazolidinedione partial PPARγ agonist elicited ~25% of the maximal efficacy of the full PPARγ agonist rosiglitazone. In the presence of the non-thiazolidinedione partial PPARγ agonist, the transcriptional activity of the full agonist, rosiglitazone, was blunted, indicating that the non-thiazolidinedione partial PPARγ agonist inhibits rosiglitazone-induced PPARγ activity. The non-thiazolidinedione partial PPARγ agonist (0.1-10 μM) inhibited vascular smooth muscle cell growth which was accompanied by an inhibition of retinoblastoma protein phosphorylation. Mitogen-induced downregulation of the cyclin-dependent kinase (CDK) inhibitor p27kip1, and induction of the G1 cyclins cyclin D1, cyclin A, and cyclin E were also attenuated by the non-thiazolidinedione partial PPARγ agonist. Maximal

antiproliferative activity of the non-thiazolidinedione partial PPARγ agonist required functional PPARγ as adenovirus-mediated overexpression of a dominant-neg. PPARγ mutant partially reversed its inhibition of vascular smooth muscle cell growth. In contrast, overexpression of dominant-neg. PPARγ did not reverse the inhibitory effect of the non-thiazolidinedione partial PPARγ agonist on cyclin D1. As the full PPARγ agonist rosiglitazone exhibited no effect on cyclin D1, inhibition of that G1 cyclin by the non-thiazolidinedione partial PPARγ agonist likely occurred through a PPARγ-independent mechanism. These data demonstrate that a non-thiazolidinedione partial PPARγ agonist may constitute a novel therapeutic for proliferative vascular diseases and could provide addnl. evidence for the important role of PPARγ in regulating vascular smooth muscle cell proliferation.

IT **118414-59-8**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(non-thiazolidinedione PPARγ ligand inhibits vascular smooth muscle cell growth)

RN 118414-59-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 5-chloro-1-[(4-chlorophenyl)methyl]-3-(phenylthio)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

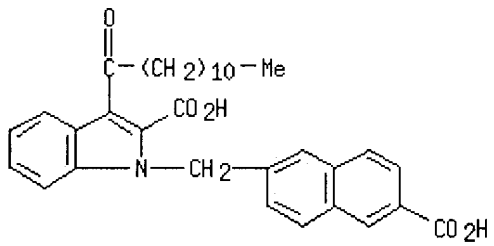
ACCESSION NUMBER: 2003:221341 HCAPLUS
DOCUMENT NUMBER: 139:111060
TITLE: Structure-activity relationship studies of 1-substituted 3-dodecanoylindole-2-carboxylic acids as inhibitors of cytosolic phospholipase A2-mediated arachidonic acid release in intact platelets
AUTHOR(S): Griessbach, Klaus; Klimt, Monika; Elfringhoff, Alwine Schulze; Lehr, Matthias
CORPORATE SOURCE: Institute of Pharmaceutical and Medicinal Chemistry, University of Munster, Munster, D-48149, Germany
SOURCE: Archiv der Pharmazie (Weinheim, Germany) (2003), Volume Date 2002, 335(11-12), 547-555
CODEN: ARPMAS; ISSN: 0365-6233
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:111060

AB A series of 3-dodecanoylindole-2-carboxylic acid derivs. with varied carboxylic acid substituents at the indole 1-position were synthesized and evaluated for their ability to inhibit arachidonic acid release in human platelets mediated by the cytosolic phospholipase A2. Structure-activity relationship studies revealed that increasing the polarity of these substituents by the introduction of addnl. polar groups in the proximity of the carboxylic acid moiety reduced activity. Conformational restriction of the indole-1-carboxylic acid substituents in distinct positions as well as extending the length of these residues led to compds. which did not substantially differ in their potencies.

IT **562813-01-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(3-dodecanoylindole-2-carboxylic acid derivs. as cytosolic phospholipase A2 inhibitors and anti-inflammatory agents)

RN 562813-01-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(6-carboxy-2-naphthalenyl)methyl]-3-(1-oxododecyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

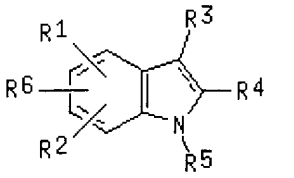
Full Text | Citing References

ACCESSION NUMBER: 2003:1275 HCAPLUS
DOCUMENT NUMBER: 138:55866
TITLE: Preparation of indole derivatives as phospholipase enzyme inhibitors for treatment of inflammatory conditions
INVENTOR(S): Seehra, Jasbir S.; McKew, John C.; Lovering, Frank; Bemis, Jean E.; Xiang, Yibin; Chen, Lihren; Knopf, John L.
PATENT ASSIGNEE(S): Genetics Institute, LLC, USA
SOURCE: U.S., 57 pp., Cont.-in-part of U. S. Ser. No. 256,062, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

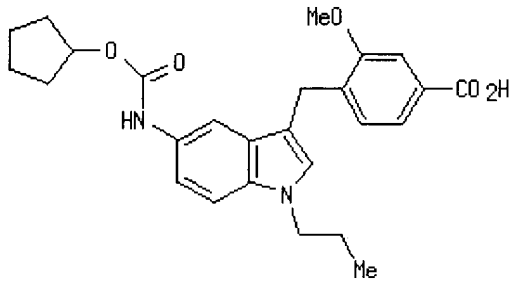
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6500853	B1	20021231	US 2000-686616	20001011

PRIORITY APPLN. INFO.: US 1998-113674P P 19980228
US 1999-256062 B2 19990224

OTHER SOURCE(S): MARPAT 138:55866
GI



I



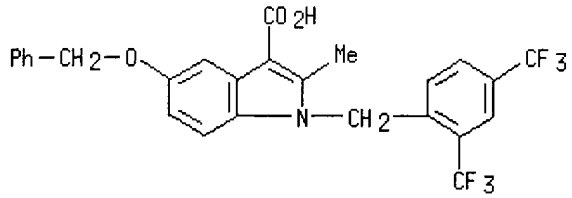
II

AB Title compds. I [wherein R1 and R6 = independently H, halo, CF3, alkyl, alkylthio, alkoxy, CN, NO2, NH2, Ph, OPh, SPh, CH2Ph, OCH2Ph, SCH2Ph, or (un)substituted amido, carbamido, sulfonyl, etc.; R2 = H, halo, CF3, OH, alkyl, alkoxy, CHO, CN, NO2, (un)substituted amino, or alkylsulfonyl; R3 = CO2H, OPO3H2, SO3H, etc.; R4 = H, CF3, alkyl, alkoxy, (alkyl)cycloalkyl, CHO, halo, etc.; R5 = alkyl, alkoxy, (alkyl)cycloalkyl, etc.; and pharmaceutically acceptable salts thereof] were prepd. as phospholipase enzyme inhibitors. For example, 5-nitroindole was C3-alkylated (55%) with Me 4-(bromomethyl)-3-methoxybenzoate in dioxane, N-alkylated (57%) with 1-iodopropane in a soln. of THF and NaH, and converted to the amine (80%) by hydrogenation using Pt/C. The amine was converted to the carbamate (39%) by addn. of cyclopentyl chloroformate in CH2Cl2 and 4-methylmorpholine, and the resultant ester was hydrolyzed to yield II (71%). The latter inhibited cytosolic phospholipase A2 (cPLA2) by 50% at a concn. of 170 μM in a coumarin assay and reduced footpad vol. by 16.61% at a dose of 5 mg/Kg IV in a carrageenan-induced footpad edema test on rats. Thus, I are useful for treatment of inflammatory conditions, such as arthritis, inflammatory bowel disease, and asthma (no data).

IT **241497-82-5P**, 1H-Indole-3-carboxylic acid, 1-[[2,4-bis(trifluoromethyl)phenyl]methyl]-2-methyl-5-(phenylmethoxy)-
RL: PAC (Pharmacological activity); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(phospholipase inhibitor; prepn. of indole derivs. as phospholipase enzyme inhibitors for treatment of inflammatory conditions)

RN 241497-82-5 HCAPLUS

CN 1H-Indole-3-carboxylic acid, 1-[[2,4-bis(trifluoromethyl)phenyl]methyl]-2-methyl-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:964145 HCAPLUS
DOCUMENT NUMBER: 138:19491
TITLE: A method for treating inflammatory diseases by administering a PPAR-δ agonist
INVENTOR(S): Forrest, Michael J.; Berger, Joel P.; Moller, David E.; Wright, Samuel
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002100351	A2	20021219	WO 2002-US20974	20020607
WO 2002100351	A3	20030501		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1399151	A2	20040324	EP 2002-746824	20020607

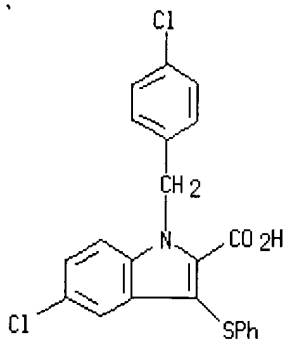
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 2001-297356P P 20010611
WO 2002-US20974 W 20020607

AB A method for treating, controlling, preventing or reducing the risk of contracting an inflammatory disease or condition in a mammalian patient, comprises (1) selecting a patient in need thereof, and (2) treating the patient with a therapeutically effective amt. of a compn. comprising a PPAR-δ agonist. Inflammatory diseases that may be treated by this method include but are not limited to rheumatoid arthritis, juvenile rheumatoid arthritis, systemic lupus erythematosus, osteoarthritis, degenerative joint disease, one or more connective tissue diseases, ankylosing spondylitis, and bursitis.

IT **118414-59-8**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(PPAR-δ agonist for treating inflammatory disease, and use with other agents)

RN 118414-59-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 5-chloro-1-[(4-chlorophenyl)methyl]-3-(phenylthio)- (9CI) (CA INDEX NAME)



10

L14 ANSWER 8 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:372413 HCAPLUS
DOCUMENT NUMBER: 137:103402
TITLE: Design and Quantitative Structure-Activity Relationship of 3-Amidinobenzyl-1H-indole-2-carboxamides as Potent, Nonchiral, and Selective Inhibitors of Blood Coagulation Factor Xa
AUTHOR(S): Matter, Hans; Defossa, Elisabeth; Heinelt, Uwe; Blohm, Peter-Michael; Schneider, Detlev; Mueller, Andrea; Herok, Silke; Schreuder, Herman; Liesum, Alexander; Brachvogel, Volker; Loenze, Petra; Walser, Armin; Al-Obeidi, Fahad; Wildgoose, Peter
CORPORATE SOURCE: DI&A Molecular Modeling Medicinal Chemistry Structural Biology DG Thrombosis and Degenerative Joint Diseases, Aventis Pharma Deutschland GmbH, Frankfurt am Main, D-65926, Germany
SOURCE: Journal of Medicinal Chemistry (2002), 45(13), 2749-2769
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of 138 nonchiral 3-amidinobenzyl-1H-indole-2-carboxamides and analogs as inhibitors of the blood coagulation enzyme factor Xa (FXa) were designed, synthesized, and investigated by X-ray structure anal. and 3D quant. structure-activity relationship (QSAR) studies (CoMFA, CoMSIA) in order to identify important protein-ligand interactions responsible for biol. affinity and selectivity. Several compds. from this series are highly potent and selective inhibitors of this important enzyme linking extrinsic and intrinsic coagulation pathways. To rationalize biol. affinity and to provide guidelines for further design, all compds. were docked into the factor Xa binding site. Those docking studies were based on X-ray structures of factor Xa in complex with literature-known inhibitors. It was possible to validate those binding modes by four X-ray crystal structures of representative ligands in factor Xa, while one ligand was addnl. crystd. in trypsin to rationalize requirements for selective factor Xa inhibition. The 3D-QSAR models based on a superposition rule derived from these docking studies were validated using conventional and cross-validated r2 values using the leave-one-out method and repeated analyses using two randomly chosen cross-validation groups plus randomization of biol. activities. This led to consistent and highly predictive 3D-QSAR models with good correlation coeffs. for both CoMFA and CoMSIA, which were found to correspond to exptl. detd. factor Xa binding site topol. in terms of steric, electrostatic, and hydrophobic complementarity. Subsets selected as smaller training sets using 2D

fingerprints and max. dissimilarity methods resulted in 3D-QSAR models with remarkable correlation coeffs. and a high predictive power. The final quant. SAR information agrees with all exptl. data for the binding topol. and thus provides reasonable activity predictions for novel factor Xa inhibitors.

IT **229950-27-0P**

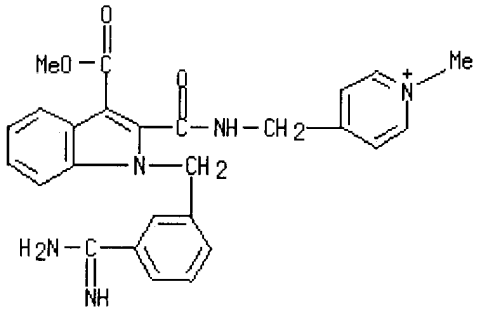
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(amidinobenzylindolecarboxamides structure-based design and QSAR as potent, nonchiral, and selective inhibitors of blood coagulation Factor Xa)

RN 229950-27-0 HCAPLUS

CN Pyridinium, 4-[[[[1-[[3-(aminoiminomethyl)phenyl]methyl]-3-(methoxycarbonyl)-1H-indol-2-yl]carbonyl]amino]methyl]-1-methyl-, salt with trifluoroacetic acid (1:1) (9CI) (CA INDEX NAME)

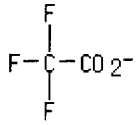
CM 1

CRN 229950-26-9
CMF C26 H26 N5 O3



CM 2

CRN 14477-72-6
CMF C2 F3 O2



REFERENCE COUNT: 97 THERE ARE 97 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

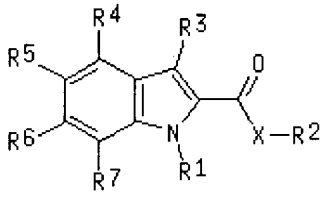
ACCESSION NUMBER: 2002:293620 HCAPLUS
DOCUMENT NUMBER: 136:309846
TITLE: Preparation of substituted indoles as PPAR-γ binding agents
INVENTOR(S): Stolle, Andreas; Dumas, Jacques P.; Carley, William; Coish, Phillip D. G.; Magnuson, Steven R.; Wang, Yamin; Nagarathnam, Dhanapalan; Lowe, Derek B.; Su, Ning; Bullock, William H.; Campbell, Ann-Marie; Qi, Ning; Baryza, Jeremy L.; Cook, James H.

PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 233 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030895	A1	20020418	WO 2001-US42644	20011009
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002011901	A5	20020422	AU 2002-11901	20011009
US 2003087902	A1	20030508	US 2001-974319	20011009
EP 1341761	A1	20030910	EP 2001-979996	20011009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2003001619	A	20030602	NO 2003-1619	20030409

PRIORITY APPLN. INFO.: US 2000-239195P P 20001010
US 2000-243665P P 20001027
WO 2001-US42644 W 20011009

OTHER SOURCE(S): MARPAT 136:309846
GI

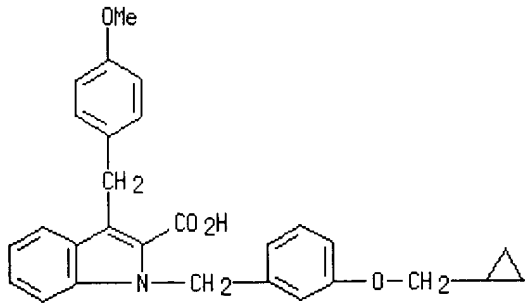


I

AB The title compds. [I; R1 = R8R9; R8 = alkyl, alkenyl, alkynyl, etc.; R9 = (un)substituted Ph, cycloalkyl, heterocycloalkyl, etc.; X = (un)substituted NH, S, O; R2 = H, alkyl, halo, alkyl, etc.; R3 = R12R13; R12 = alkyl, alkenyl, alkynyl, CO; R13 = (un)substituted cycloalkyl, cycloalkenyl, heterocycloalkyl, etc.; R4-R7 = H, OH, etc.], useful in treating or preventing PPAR-γ mediated diseases or conditions, such as osteopenia, osteoporosis, cancer, diabetes and atherosclerosis, were prepd. Thus, hydrolysis of Et 3-(cyclopropylidenemethyl)-1-[3-(trifluoromethyl)benzyl]-1H-indole-2-carboxylate (prepn. given) with NaOH in H2O/THF afforded 57% I [R1 = 3-F3CC6H4CH2; X = O; R2 = H; R3 = cyclopropylidenemethyl; R4-R7 = H] which showed IC50 of 100 pM and 9.99 nM against PPAR-γ binding.

IT **412004-67-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted indoles as PPAR-γ binding agents)

RN 412004-67-2 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[[3-(cyclopropylmethoxy)phenyl]methyl]-3-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

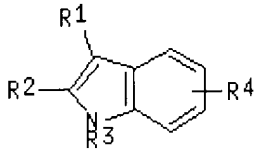
L14 ANSWER 10 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:213824 HCAPLUS
DOCUMENT NUMBER: 136:247492
TITLE: Preparation of indolecarboxylates as neoplasm inhibitors.
INVENTOR(S): Pamukcu, Rifat; Piazza, Gary A.
PATENT ASSIGNEE(S): Cell Pathways, Inc., USA
SOURCE: U.S., 45 pp., Cont. of U.S. Ser. No. 200,139, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6358992	B1	20020319	US 1999-443395	19991119

PRIORITY APPLN. INFO.: US 1998-200139 B1 19981125
OTHER SOURCE(S): MARPAT 136:247492
GI



I

Apparently compound reason it= Put not inflammatory disease

AB Claimed is a method of treating a mammal having precancerous lesions comprising administration of title compds. [I; R1 = H, halo, NO2, (protected) carboxy, acyl, cyano, hydroxyiminoalkyl, alkenyl optionally substituted with oxo, alkyl optionally substituted with protected carboxy, carboxy, OH ; R2 = H, halo, alkenyl, acyl, alkyl optionally substituted with protected carboxy, carboxy, alkoxy, OH; R1R2 = atoms to form a 4-7 membered (oxo)carbocyclic ring; R3 = (substituted) alkenyl, alkyl; R4 = (protected) carboxy, acyl, cyano, halo, heterocyclyl, amino optionally substituted with acyl or protected carboxy, alkyl optionally substituted with (protected) carboxy, acyl] (no data). Thus, Me 3-acetyl-2-

propylindole-6-carboxylate in DMF was treated with NaH then with 2-chlorobenzyl bromide followed by stirring for 1 h to give Me 3-acetyl-1-(2-chlorobenzyl)-2-propylindole-6-carboxylate.

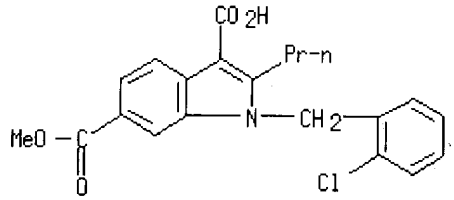
IT **184149-02-8P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of indolecarboxylates as neoplasm inhibitors)

RN 184149-02-8 HCAPLUS

CN 1H-Indole-3,6-dicarboxylic acid, 1-[(2-chlorophenyl)methyl]-2-propyl-, 6-methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 11 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:885732 HCAPLUS
DOCUMENT NUMBER: 136:11205
TITLE: Combinations of an endothelin receptor antagonist and an antiepileptic compound having analgesic activity
INVENTOR(S): Dooley, David James
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001091736	A2	20011206	WO 2001-US14793	20010508
WO 2001091736	A3	20021017		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1289558	A2	20030312	EP 2001-939002	20010508
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001011207	A	20030401	BR 2001-11207	20010508
JP 2003535061	T2	20031125	JP 2001-587752	20010508
US 2003232787	A1	20031218	US 2002-296792	20021126

PRIORITY APPLN. INFO.: US 2000-208259P P 20000531
WO 2001-US14793 W 20010508

OTHER SOURCE(S): MARPAT 136:11205

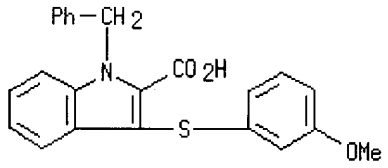
AB The present invention is a novel combination effective for alleviating pain comprising an endothelin receptor antagonist or a salt and from 1 to 3 compds. independently selected from the group consisting of antiepileptics having analgesic activity, and pharmaceutical compns. comprising the compds. The administration of endothelin receptor antagonists in these novel combinations results in an improved redn. in the frequency and severity of pain. The incidence of unwanted side effects can be reduced by these novel combinations in comparison to using higher doses of a single agent treatment to achieve a similar therapeutic effect. Thus, tablets contained 4-(7-ethyl-1,3-benzodioxol-5-yl)-2-[2-(trifluoromethyl)phenyl]-2H-1,2-dihydro-1,2-benzothiazine-3-carboxylic acid 1,1-dioxide potassium salt 25, gabapentin 25, lactose 50, corn starch (for mix) 10, corn starch (paste) 10, and Mg stearate 5 mg. The combinations of the present invention are effective at reversing static allodynia,and are thus useful for the treatment of pain.

IT 175339-72-7

RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(combinations of endothelin receptor antagonist and antiepileptic having analgesic activity)

RN 175339-72-7 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 3-[(3-methoxyphenyl)thio]-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 12 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:661388 HCAPLUS
DOCUMENT NUMBER: 135:226878
TITLE: Synthesis of N-benzyl-indolyl(benzyloxy)amido derivatives as PDE-IV inhibitors
INVENTOR(S): Labelle, Marc; Sturino, Claudio; Lachance, Nicolas; MacDonald, Dwight
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001064639	A2	20010907	WO 2001-CA270	20010302
WO 2001064639	A3	20020228		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

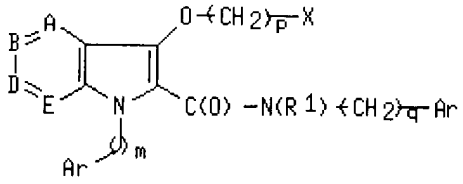
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002068756	A1	20020606	US 2001-797083	20010301
US 6436965	B2	20020820		
EP 1263728	A2	20021211	EP 2001-913422	20010302
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003525273	T2	20030826	JP 2001-563482	20010302

PRIORITY APPLN. INFO.: US 2000-186571P P 20000302
WO 2001-CA270 W 20010302

OTHER SOURCE(S): MARPAT 135:226878

GI



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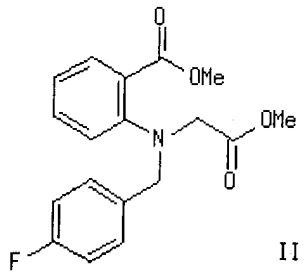

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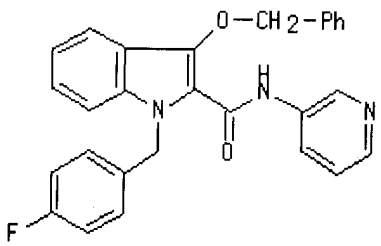


III

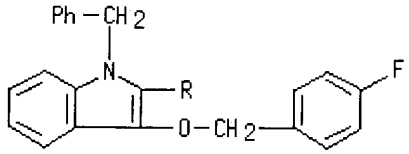
AB Title compds. I [A, B, D, E = N or CR2 and the others = CR2; q = 0 - 1; p, m = 0 - 2; R1 = H, (hydroxy)alkyl; R2 = H, halo, (halo)alkyl, hydroxyalkyl, CN, arom. or nonarom. ring system contg. 1 - 4 heteroatoms selected from O, S, N, alkoxy, oxyamide, etc.; X = cycloalkyl or Ar; Ar = (un)substituted (Ph, thienyl, thiazolyl, pyridyl, oxazolyl, tetrazolyl, pyrimidinyl, pyrazinyl and pyridazinyl)]were prepd. Over 150 compds. were disclosed. For instance, Me 2-aminobenzoate was alkylated with 4-fluorobenzyl bromide (K2CO3, MEK, reflux, 8 h.). The resulting ester was sapond. (NaOH, MeOHaq reflux, 2 h.), N-alkylated with Me bromoacetate (K2CO3, MeOHaq, reflux, 18 h.) and treated with CH2N2 to afford II. Diester II was cyclized (NaOMe, MeOH, reflux, 30 min.), O-alkylated with benzyl bromide (K2CO3, MEK, reflux, 2 h.), sapond. (NaOH, EtOHaq, 90°C, 40 min.) and finally coupled to 3-aminopyridine (SOCl2, i-Pr2NEt, room temp., 3 h.) to yield III. I are PDE-IV inhibitors (no data) useful for treating, e.g., inflammation, muscle spasm, chronic bronchitis, etc.

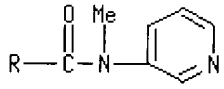
IT **359001-30-2P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; synthesis of N-benzyl-indolyl(benzyloxy)amido derivs. as PDE-IV inhibitors)

RN 359001-30-2 HCAPLUS

CN 1H-Indole-2-carboxamide, 3-[(4-fluorophenyl)methoxy]-N-methyl-1-(phenylmethyl)-N-3-pyridinyl- (9CI) (CA INDEX NAME)





L14 ANSWER 13 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

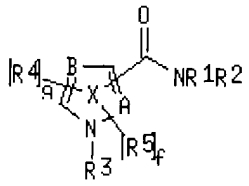
Full Text | Citing References

ACCESSION NUMBER: 2001:597958 HCAPLUS
DOCUMENT NUMBER: 135:166827
TITLE: Preparation of 1H-indole-3-carboxamides, 1H-indazole-3-carboxamides, 1H-pyrido[4,3-b]indol-1-ones and pyrrolo[1,2,3-de]-1,4-benzoxazine-6-carboxamides as cannabinoid receptor modulators for treating respiratory and non-respiratory diseases
INVENTOR(S): Leftheris, Katerina; Zhao, Rulin; Chen, Bang-Chi; Kiener, Peter; Wu, Hong; Pandit, Chennagiri R.; Wrobleski, Stephen; Chen, Ping; Hynes, John, Jr.; Longphre, Malinda; Norris, Derek J.; Spergel, Steven; Tokarski, John
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA; et al.
SOURCE: PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001058869	A2	20010816	WO 2001-US4131	20010208
WO 2001058869	A3	20020124		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1254115	A2	20021106	EP 2001-907144	20010208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004502642	T2	20040129	JP 2001-558420	20010208

PRIORITY APPLN. INFO.: US 2000-181818P P 20000211
WO 2001-US4131 W 20010208

OTHER SOURCE(S): MARPAT 135:166827
GI



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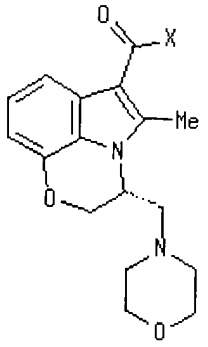


II

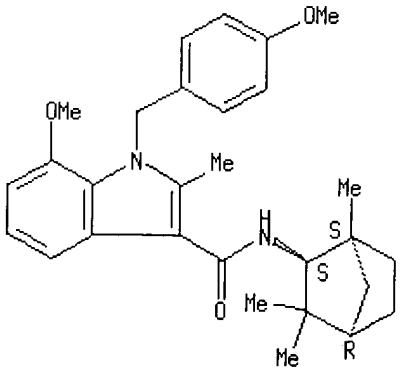
AB The title compds. [I; A, B = C, N so that ring X = pyrrole, pyrazole or imidazole (wherein when A = N, the group CONR1R2 is attached to atom C-3 and R5 does not exist; and when A = C, one of CONR1R2 and R5 is attached to A and the other to atom C-3; and when B = C, two R4 groups attached to B and atom C-5, resp., form a fused 6-membered hetroaryl); f = 0-1; g = 1-2; R1, R2 = H, alkyl, heterocycloalkyl, etc.; R2 together with R1 or R5 forms a 5-6 membered heterocyclo; R3 = H, alkyl, aryl, etc.; R4 is attached to atom C-5 and optionally B and is H, alkyl, aryl, etc.; R5 is attached to A or atom C-3 and is H, alkyl, aryl, etc.; R5 together with R2 forms a heterocyclo], useful as cannabinoid receptor modulators (no data given) for treating respiratory and non-respiratory leukocyte-activation assocd. diseases, were prepd. Thus, reacting the acid chloride II [X = Cl] (multi-step synthesis given) with 2,2,6,6-tetramethylcyclohexylamine afforded the pyrrolo[1,2,3-de]-1,4-benzoxazine-6-carboxamide II [X = 2,2,6,6-tetramethylcyclohexylamino].

IT **354569-79-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 1H-indole-3-carboxamides, 1H-indazole-3-carboxamides, 1H-pyrido[4,3-b]indol-1-ones and pyrrolo[1,2,3-de]-1,4-benzoxazine-6-carboxamides as cannabinoid receptor modulators for treating respiratory and non-respiratory diseases)

RN 354569-79-2 HCAPLUS

CN 1H-Indole-3-carboxamide, 7-methoxy-1-[(4-methoxyphenyl)methyl]-2-methyl-N-[(1S,2S,4R)-1,3,3-trimethylbicyclo[2.2.1]hept-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 14 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:319722 HCAPLUS
DOCUMENT NUMBER: 134:320871
TITLE: Pharmaceuticals for treating obesity containing antagonists and partial agonists of PPAR-γ
INVENTOR(S): Berger, Joel P.; Doebber, Thomas W.; Leibowitz, Mark; Moller, David E.; Mosley, Ralph T.; Tolman, Richard L.; Ventre, John; Zhang, Bei B.; Zhou, Gaochao
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001030343	A1	20010503	WO 2000-US28924	20001019
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1284728	A1	20030226	EP 2000-973670	20001019
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003525217	T2	20030826	JP 2001-532763	20001019
US 2003032581	A1	20030213	US 2002-241106	20020911

PRIORITY APPLN. INFO.:

US 1999-161225P	P	19991022
US 2000-691955	A3	20001019
WO 2000-US28924	W	20001019

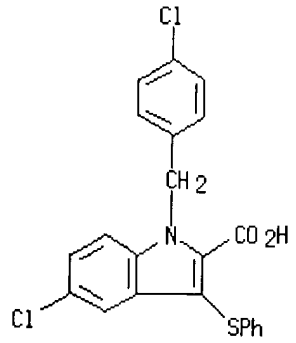
OTHER SOURCE(S): MARPAT 134:320871

AB Compds. which are antagonists of strong PPAR-γ agonists, such as rosiglitazone, and are also partial agonists of the PPAR-γ receptor, are active agents for correcting or reducing obesity. For example, 1-(p-chlorobenzyl)-5-chloro-3-thiophenylindole-2-carboxylic acid, is characterized as being a potent and selective ligand for PPAR-γ which has partial agonist (<30 maximal effects relative to rosiglitazone) and antagonist activity in cell-free and cell-based assays for the PPAR-γ receptor. The compd. is a potent agent for reducing obesity and insulin resistance in fat-fed C57BL/6J mice. This compd. and other PPAR-γ antagonists/partial agonists and pharmaceutically acceptable salts are effective in the treatment of obesity and related disorders, such as diabetes, insulin resistance, hyperlipidemia, atherosclerosis, inflammation and cancer.

IT **118414-59-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(compns. contg. PPAR-γ receptor antagonists/partial agonists for treatment of obesity and related disorders)

RN 118414-59-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 5-chloro-1-[(4-chlorophenyl)methyl]-3-

(phenylthio)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 15 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:666700 HCAPLUS
DOCUMENT NUMBER: 133:252170
TITLE: Preparation of novel N-cyanomethyl amides as protease inhibitors
INVENTOR(S): Bryant, Clifford M.; Bunin, Barry A.; Kraynack, Erica A.; Patterson, John W.
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055125	A2	20000921	WO 2000-US6747	20000315
WO 2000055125	A3	20010426		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000009042	A	20011226	BR 2000-9042	20000315
EP 1178958	A2	20020213	EP 2000-916343	20000315
EP 1178958	B1	20040218		
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TR 200103390	T2	20020521	TR 2001-20010339	20000315
US 6455502	B1	20020924	US 2000-526090	20000315
TR 200201874	T2	20021021	TR 2002-20020187	20000315
US 6476026	B1	20021105	US 2000-526485	20000315
JP 2002539191	T2	20021119	JP 2000-605556	20000315
EE 200100485	A	20030217	EE 2001-485	20000315

NZ 514234	A	20040227	NZ 2000-514234	20000315
AT 259782	E	20040315	AT 2000-916343	20000315
ZA 2001007494	A	20020911	ZA 2001-7494	20010911
ZA 2001007495	A	20020911	ZA 2001-7495	20010911
NO 2001004485	A	20011105	NO 2001-4485	20010914
BG 106003	A	20020628	BG 2001-106003	20011010
HR 2001000738	A1	20021231	HR 2001-738	20011012
US 2002086996	A1	20020704	US 2001-17851	20011214
US 6593327	B2	20030715		
US 2003096796	A1	20030522	US 2002-205600	20020724
US 2003119788	A1	20030626	US 2002-241001	20020909

PRIORITY APPLN. INFO.:

US 1999-124420P	P	19990315
US 2000-526090	A1	20000315
US 2000-526485	A3	20000315
WO 2000-US6747	W	20000315

OTHER SOURCE(S): MARPAT 133:252170

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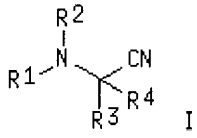
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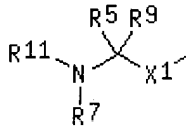
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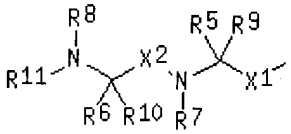
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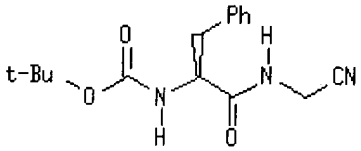

IV

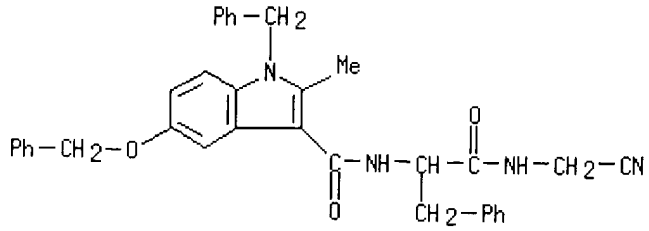
AB The title compds. [I; R1 = II, III (wherein X1, X2 = CO, CH2SO2; R5, R6 = H, alkyl; R7, R8 = H, alkyl, etc.; R9, R10 = alkyl optionally substituted with CN, halo, NO2, etc.; R11 = X5X6R18; X5 = CO, COCO, SO2; X6 = a bond, O, NH, N(alkyl); R18 = alkyl optionally substituted with CN, halo, NO2, etc.); R2 = H, alkyl, etc.; R3 = H, alkyl, etc.; R4 = H, alkyl optionally substituted with CN, halo, NO2, etc.; R4 and R2 taken together form trimethylene, tetramethylene, phenylene-1,2-dimethylene, optionally substituted with hydroxy, oxo or methylene; R4 and R3 together with the carbon atom to which both are attached form cycloalkylene, heterocycloalkylene], useful for treating diseases assocd. with cysteine protease activity, particularly diseases assocd. with activity of cathepsins B, K, L or S such as inflammation and asthma, were prepd. and formulated. Thus, reacting 2(S)-tert-butoxycarbonylamino-3-phenylpropionic acid with aminoacetonitrile.HCl in the presence of Et3N in DMF and MeCN afforded the amide (1S)-IV. Biol. data for compds. I were given.

IT **294640-68-9P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of novel N-cyanomethyl amides as protease inhibitors)

RN 294640-68-9 HCAPLUS

CN 1H-Indole-3-carboxamide, N-[2-[(cyanomethyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-2-methyl-5-(phenylmethoxy)-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 16 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

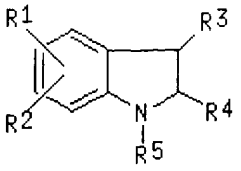
Full Text | Citing References

ACCESSION NUMBER: 1999:566026 HCAPLUS
DOCUMENT NUMBER: 131:199619
TITLE: Preparation of indole derivatives as phospholipase enzyme inhibitors
INVENTOR(S): Seehra, Jasbir S.; Mckew, John C.; Lovering, Frank; Bemis, Jean E.; Xiang, Yibin; Chen, Lihren; Knopf, John L.
PATENT ASSIGNEE(S): Genetics Institute, Inc., USA
SOURCE: PCT Int. Appl., 182 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943654	A2	19990902	WO 1999-US3898	19990224
WO 9943654	A3	19991028		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2322162	AA	19990902	CA 1999-2322162	19990224
AU 9927825	A1	19990915	AU 1999-27825	19990224
AU 765427	B2	20030918		
BR 9908275	A	20001024	BR 1999-8275	19990224
TR 200002447	T2	20001121	TR 2000-200002447	19990224
EP 1062205	A2	20001227	EP 1999-908378	19990224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002504541	T2	20020212	JP 2000-533412	19990224
EE 200000488	A	20020215	EE 2000-488	19990224
NO 2000004219	A	20001023	NO 2000-4219	20000823
HR 2000000551	A1	20010430	HR 2000-551	20000824
BG 104779	A	20011031	BG 2000-104779	20000919

PRIORITY APPLN. INFO.: US 1998-30592 A 19980225
WO 1999-US3898 W 19990224

OTHER SOURCE(S): MARPAT 131:199619
GI



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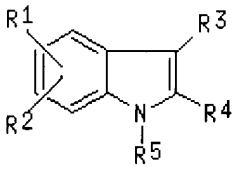

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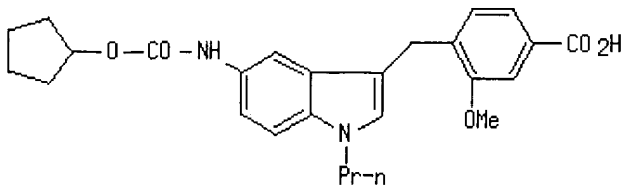


III

AB Indole derivs. (I) and (II) [where R1 = H, halogen, CF3, C1-10 alkyl, S-C1-10 alkyl, C1-10 alkoxy, CN, NO2, NH2, Ph, OPh, SPh, CH2Ph, OCH2Ph, SCH2Ph, or (un)substituted amido, carbamido, sulfonyl, etc.; R2 = H, halogen, CF3, OH, C1-10 alkyl, C1-10 alkoxy, CHO, CN, NO2, (un)substituted amino, SO2-C1-6 alkyl; R3 = (un)substituted carboxylic acid, OPO3H2, SO3H, etc.; R4 = H, CF3, C1-6 alkyl, C1-6 alkoxy, (C1-6 alkyl)cycloalkyl, CHO, halogen, etc.; R5 = C1-6 alkyl, C1-6 alkoxy, (C1-6 alkyl)cycloalkyl, etc.] and pharmaceutically acceptable salts thereof, were prepd. by several methods. Thus, 5-nitroindole was C3-alkylated with Me 4-(bromomethyl)-3-methoxybenzoate in dioxane, N-alkylated with 1-iodopropane in a soln. of THF and NaH, and converted to the amine by hydrogenation over Pt/C. The amine was converted to the carbamate by addn. of cyclopentyl chloroformate in CH2Cl2 and 4-methylmorpholine and the resultant ester hydrolyzed to yield 4-[(5-{[(cyclopentyloxy)carbonyl]amino}-1-propyl-1H-indol-3-yl)methyl]-3-methoxybenzoic acid (III). The title compds. are useful as phospholipase enzyme inhibitors, esp. cytosolic phospholipase A2 (cPLA2), for treatment of inflammatory conditions, particularly where inhibition of prodn. of prostaglandins, leukotrienes, and PAF are all desired. Over one hundred compds. of the invention were tested for cPLA2 inhibiting activity in the Coumarine assay and rat carrageenan-induced footpad edema test. Compds. exhibited 7% to 98% inhibition at concns. of 0.125 μM to 400 μM in the Coumarine assay and -7.16% to 34.52% inhibition at concns. of 2 μM to 20 μM in the footpad edema test.

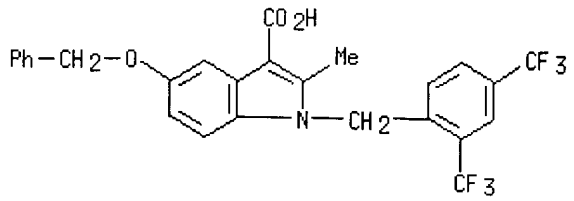
IT **241497-82-5P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of indole derivs. as phospholipase enzyme inhibitors for treatment of inflammatory conditions)

RN 241497-82-5 HCAPLUS

CN 1H-Indole-3-carboxylic acid, 1-[[2,4-bis(trifluoromethyl)phenyl]methyl]-2-methyl-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



L14 ANSWER 17 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

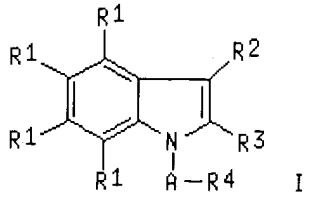
Full Text | Citing References

ACCESSION NUMBER: 1999:460399 HCAPLUS
DOCUMENT NUMBER: 131:87814
TITLE: Indole derivatives as inhibitors of factor Xa, and their preparation and use as anticoagulants
INVENTOR(S): Defossa, Elisabeth; Heinelt, Uwe; Klingler, Otmar; Zoller, Gerhard; Al-Obeidi, Fahad; Walser, Armin; Wildgoose, Peter; Matter, Hans
PATENT ASSIGNEE(S): Hoechst Marion Roussel Deutschland GmbH, Germany
SOURCE: PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9933800	A1	19990708	WO 1998-EP8030	19981210
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2316172	AA	19990708	CA 1998-2316172	19981210
AU 9920528	A1	19990719	AU 1999-20528	19981210
AU 743881	B2	20020207		
BR 9814340	A	20001003	BR 1998-14340	19981210
EP 1042287	A1	20001011	EP 1998-965244	19981210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI				
TR 200001954	T2	20001221	TR 2000-20000195	19981210
JP 2001527066	T2	20011225	JP 2000-526484	19981210
NZ 505370	A	20020628	NZ 1998-505370	19981210
RU 2225397	C2	20040310	RU 2000-119774	19981210
ZA 9811759	A	19990728	ZA 1998-11759	19981222
NO 2000003057	A	20000818	NO 2000-3057	20000614
US 6337344	B1	20020108	US 2000-582344	20000814

PRIORITY APPLN. INFO.: EP 1997-122901 A 19971224
WO 1998-EP8030 W 19981210

OTHER SOURCE(S): MARPAT 131:87814
GI



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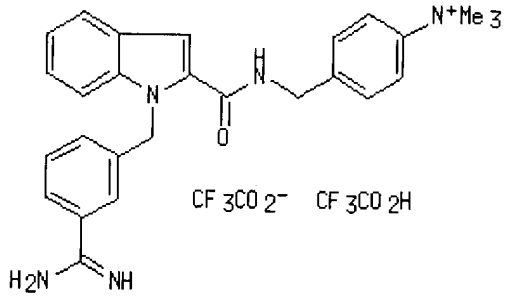


II

AB The invention relates to the inhibition of blood clotting proteins, and more particularly, to indole derivs. or their physiol. acceptable salts which effect this, having formula I [R1 groups = H, halo, alkyl, CF3, (un)substituted Ph or phenylalkoxy, etc., with ≥2 of R1 being H; ≥1 of R2 and R3 = (CH2)0-2CO2H or derivs., other = H, F, Cl, Br, or alkyl; or R2R3 = CH2CH2N(COPh)CH2 or analogs; A = bond, alk(en/yn)ylene, CO, SO, SO2, etc.; R4 = (un)substituted Ph, pyridyl, or other heterocyclyl]. I are inhibitors of the blood clotting enzyme factor Xa. The invention also relates to processes for the prepn. of I, to methods of inhibiting factor Xa activity and blood clotting, to use of I in the treatment and prophylaxis of assocd. (e.g., thromboembolic) diseases, and to the use of I in the prepn. of related medicaments. The invention further relates to compns. contg. I, in particular pharmaceutical compns. contg. a compd. I and pharmaceutically acceptable carriers and/or auxiliary substances. Over 160 compds. I were prepd. For instance, 1H-indole-2-carboxylic acid Et ester underwent a 5-step sequence to give title salt II. This prepn. involved (1) N-alkylation with 3-cyanobenzyl bromide, (2) alk. hydrolysis of the ester, (3) amidation with 4-(Me2N)C6H4CH2NH2.2HCl, (4) conversion of the nitrile to a thioamide, and (5) quaternization at dimethylamino, and ammonolysis of the thioamide to an amidine. In an assay using human factor Xa in vitro, II had a Ki value of 0.090 μM.

IT **229950-28-1P**

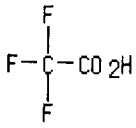
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compd.; prepn. of indole derivs. as inhibitors of factor Xa)

RN 229950-28-1 HCAPLUS

CN Pyridinium, 4-[[[[1-[[3-(aminoiminomethyl)phenyl]methyl]-3-(methoxycarbonyl)-1H-indol-2-yl]carbonyl]amino]methyl]-1-methyl-, salt with trifluoroacetic acid (1:1), mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 76-05-1
CMF C2 H F3 O2

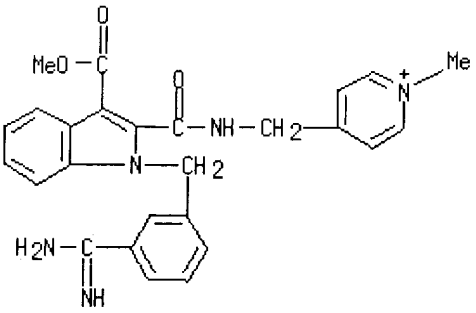


CM 2

CRN 229950-27-0
CMF C26 H26 N5 O3 . C2 F3 O2

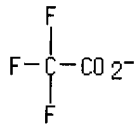
CM 3

CRN 229950-26-9
CMF C26 H26 N5 O3



CM 4

CRN 14477-72-6
CMF C2 F3 O2



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 18 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:635621 HCAPLUS
DOCUMENT NUMBER: 129:265475
TITLE: Indolecarboxamides, preparation thereof, pharmaceutical compositions, and methods of inhibiting calpain
INVENTOR(S): Daines, Robert A.; Sham, Kelvin Kin-Cheong
PATENT ASSIGNEE(S): Smithkline Beecham Corp., USA
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9841092	A1	19980924	WO 1998-US4873	19980313
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1018878	A1	20000719	EP 1998-909146	19980313
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
JP 2001515508	T2	20010918	JP 1998-540629	19980313
US 6214856	B1	20010410	US 1999-380317	19990830

PRIORITY APPLN. INFO.: US 1997-40589P P 19970314
WO 1998-US4873 W 19980313

OTHER SOURCE(S): MARPAT 129:265475

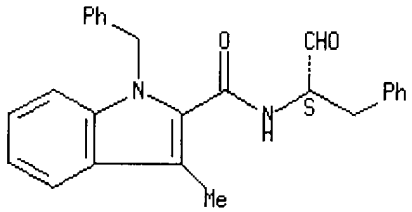
AB Pharmaceutical compns. and methods of inhibiting calpain using indolecarboxamides are disclosed. The compns. and methods of the invention are useful in the treatment of e.g. neurodegenerative disorders, strokes, and traumatic brain injury. Prepn. of e.g. (S)-N-(1-formyl-2-phenylethyl)-1-methyl-2-indolecarboxamide is described, as are capsule and other formulations.

IT **213599-01-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(indolecarboxamides, prepn., pharmaceutical compns., and methods of inhibiting calpain)

RN 213599-01-0 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[(1S)-1-formyl-2-phenylethyl]-3-methyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

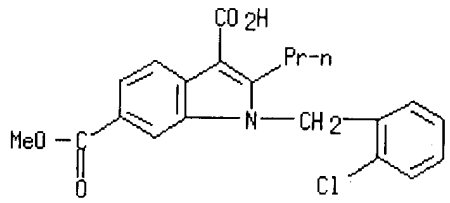
L14 ANSWER 19 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:274848 HCAPLUS
DOCUMENT NUMBER: 129:45274
TITLE: Therapeutic uses and formulations of blood sugar-lowering indoles and their uses in preparation of pharmaceuticals
INVENTOR(S): Oku, Teruo; Sawada, Kozo; Kuroda, Akio; One, Kazuhiko; Yamazaki, Noritsugu; Imoto, Takafumi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 63 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10114654	A2	19980506	JP 1996-268402	19961009

PRIORITY APPLN. INFO.: JP 1996-268402 19961009
OTHER SOURCE(S): MARPAT 129:45274
AB Pharmaceutical prepns. contg. indoles their pharmacol. acceptable salts are useful for prevention and/or treatment of glucose tolerance disorders, diabetes mellitus, hyperlipidemia, insulin resistance syndrome, cardiovascular disease, or hyperglycemia. The indoles are also useful in prepn. of pharmaceuticals. Administration of 6-benzenesulfonylcarbamoyl-1-(2-chlorobenzyl)-2-methylindole at 300 mg/kg p.o. to db/db mice showed 70% lowering of blood sugar concns.
IT **184149-02-8P**
RL: SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and therapeutic uses of blood sugar-lowering indoles)
RN 184149-02-8 HCAPLUS
CN 1H-Indole-3,6-dicarboxylic acid, 1-[(2-chlorophenyl)methyl]-2-propyl-, 6-methyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 20 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 1998:155177 HCAPLUS
DOCUMENT NUMBER: 128:275074
TITLE: Cyclic nucleotide phosphodiesterase (PDE) inhibitors for prevention and treatment of lupus erythematosus and nephritis, and indoles as cGMP-PDE inhibitors
INVENTOR(S): Nomoto, Atsushi; Hamada, Kaori; Kodama, Hiroshi; Sokabe, Keizo
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 61 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10067682	A2	19980310	JP 1997-191618	19970716

PRIORITY APPLN. INFO.: AU 1996-1188 19960723
OTHER SOURCE(S): MARPAT 128:275074
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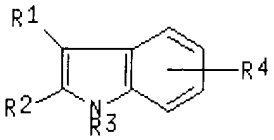


I

AB Prophylactic and therapeutic agents for (systemic) lupus erythematosus and lupus nephritis contain cyclic nucleotide PDE inhibitors as active

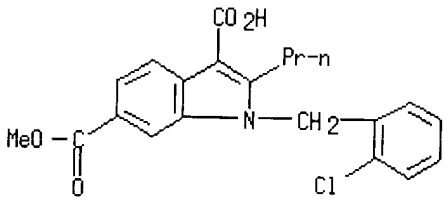
ingredients. Also claimed are indoles I [R1 = H, halo, NO2, (protected) CO2H, acyl, cyano, hydroxyimino-lower alkyl, (oxo-substituted) lower alkenyl, etc.; R2 = H, halo, lower alkenyl, acyl, (protected) CO2H, lower alkoxy, lower (hydroxy)alkyl; R3 = (un)substituted lower alkenyl, (un)substituted lower alkyl; R4 = (protected) CO2H, acyl, cyano, halo, heterocyclyl, (un)substituted NH2, (un)substituted alkyl; R1CCR2 may form (oxo-substituted) 4- to 7-membered heterocyclic ring] or their medically acceptable salts as cGMP-PDE inhibitors. 1-(6-Chloro-3,4-methylenedioxybenzyl)-3-methoxyacetyl-2-propylindole-6-carboxamide was effective in treatment of immune-complex nephritis in mice.

IT **184149-02-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of indoles as cyclic nucleotide PDE inhibitors for treatment of lupus erythematosus and nephritis)

RN 184149-02-8 HCAPLUS

CN 1H-Indole-3,6-dicarboxylic acid, 1-[(2-chlorophenyl)methyl]-2-propyl-, 6-methyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 21 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

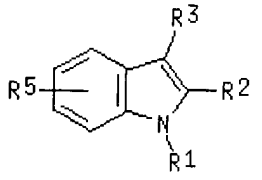
ACCESSION NUMBER: 1998:112340 HCAPLUS
DOCUMENT NUMBER: 128:167350
TITLE: Preparation of acylpyrrole- and acylindoledicarboxylic acids as phospholipase A2 inhibitors
INVENTOR(S): Lehr, Matthias
PATENT ASSIGNEE(S): Merckle G.m.b.H., Germany; Lehr, Matthias
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9805637	A1	19980212	WO 1997-EP3842	19970717
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9737679	A1	19980225	AU 1997-37679	19970717
EP 923546	A1	19990623	EP 1997-934481	19970717
EP 923546	B1	20031126		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI

JP 2000515529	T2	20001121	JP 1998-507515	19970717
AT 255090	E	20031215	AT 1997-934481	19970717
NO 9900413	A	19990128	NO 1999-413	19990128
KR 2000029658	A	20000525	KR 1999-700734	19990129
US 6310217	B1	20011030	US 1999-240148	19990129
PRIORITY APPLN. INFO.:			DE 1996-19631102 A	19960801
			WO 1997-EP3842 W	19970717

OTHER SOURCE(S): MARPAT 128:167350
GI



I

AB Title compds. [e.g., I; R1 = Y1ArY2Y3; R2 = carboxy(alkyl), alkoxycarbonyl(alkyl), carbamoyl(alkyl), etc.; R3 = alkanoyl, aroyl, etc.; R5 = H or ≥1 of halo, alkyl, alkoxy, etc.; Y1,Y2 = alk(en)ylene, etc.; Y3 = CO2H, alkoxycarbonyl, CONH2, etc.; Ar = (un)substituted arylene] were prepd. Thus, Et pyrrole-2-carboxylate was acylated and the product N-alkylated by (E)-4-(BrH2C)C6H4CH:CHCO2Et to give, after sapon., I [R1 = (E)-H2CC6H4(CH:CHCO2Et)-4, R2 = CO2H, R3 = dodecanoyl, R5 = H]. Data for biol. activity of title compds. were given.

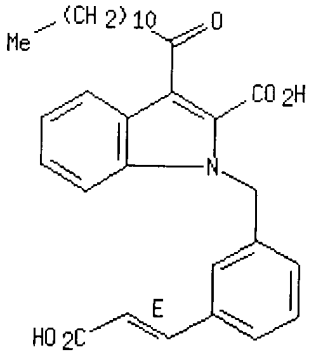
IT **192182-33-5P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of acylpyrrole- and acylindoledicarboxylic acids as phospholipase A2 inhibitors)

RN 192182-33-5 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[[3-(2-carboxyethenyl)phenyl]methyl]-3-(1-oxododecyl)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 22 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1996:746234 HCAPLUS
DOCUMENT NUMBER: 126:18786

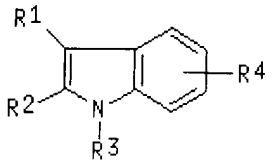
TITLE: Indole derivatives as cGMP-PDE inhibitors
INVENTOR(S): Oku, Teruo; Sawada, Kozo; Kuroda, Akio; Ohne, Kazuhiko; Nomoto, Atsushi; Hosogai, Naomi; Nakajima, Yoshimitsu; Nagashima, Akira; Sogabe, Keizo; Amura, Kouichi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co, Ltd., Japan
SOURCE: PCT Int. Appl., 211 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9632379	A1	19961017	WO 1996-JP892	19960402
CA 2217707	AA	19961017	CA 1996-2217707	19960402
AU 9651234	A1	19961030	AU 1996-51234	19960402
AU 713460	B2	19991202		
EP 820441	A1	19980128	EP 1996-907750	19960402
EP 820441	B1	20020626		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1187812	A	19980715	CN 1996-194691	19960402
JP 11503445	T2	19990326	JP 1996-530864	19960402
AT 219765	E	20020715	AT 1996-907750	19960402
ES 2175079	T3	20021116	ES 1996-907750	19960402
ZA 9602859	A	19961011	ZA 1996-2859	19960410
TW 420663	B	20010201	TW 1996-85104519	19960416
US 6069156	A	20000530	US 1997-930597	19971210

PRIORITY APPLN. INFO.:

GB 1995-7432	A	19950410
GB 1995-12560	A	19950621
GB 1995-16136	A	19950807
AU 1996-8294	A	19960227
WO 1996-JP892	W	19960402

OTHER SOURCE(S): MARPAT 126:18786
GI



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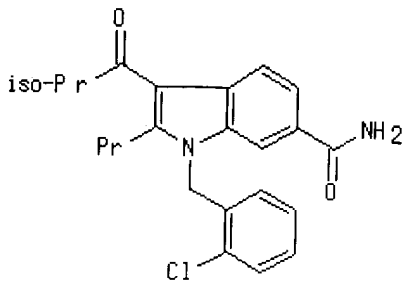


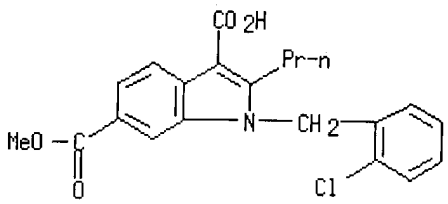
II

AB The invention relates to new indole derivs. I and their pharmaceutically acceptable salts [wherein R1 = H, halo, NO2, CO2H, protected CO2H, acyl, (un)substituted alk(en)yl, etc.; R2 = H, halo, alkenyl, acyl, (un)substituted alkyl, etc.; R3 = (un)substituted alk(en)yl where the substituent is oxo, (un)substituted aryl, or heterocyclyl; R4 = CO2H, protected CO2H, acyl, cyano, amino, halo, etc.; R1 and R2 may form 4- to 7-membered carboxylic ring (un)substituted with oxo]. I are cyclic nucleotide-PDE inhibitors (specifically cGMP-PDE), and are useful for treating and preventing a variety of conditions, including angina,

hypertension, renal failure, atherosclerosis, stroke, asthma, impotence, diabetic complications, and glaucoma. Almost 300 compds. I and numerous intermediates were prepd. For example, Me 3-isobutyryl-2-propylindole-6-carboxylate (prepn. given) was N-benzylated by 2-chlorobenzyl bromide using NaH in DMF. The product underwent sapon. with NaOH in aq. EtOH, followed by amidation of the resultant acid using EDC, HOBt, and aq. NH3, to give title amide II. II inhibited human platelet cGMP-PDE in vitro with IC50 <100 nM. I were also active in a variety of other bioassays, including relaxation of isolated rat aorta, inhibition of vascular smooth muscle cell proliferation, inhibition of vasopressin-induced vasospasm, the cyclosporin and FK506 nephritis models, the diabetic glomerulosclerosis model, and several animal impotence models.

IT **184149-02-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of indole derivs. as cGMP-PDE inhibitors)

RN 184149-02-8 HCAPLUS
CN 1H-Indole-3,6-dicarboxylic acid, 1-[(2-chlorophenyl)methyl]-2-propyl-, 6-methyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 23 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

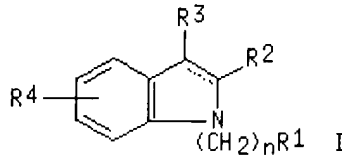
Full Text | Citing References

ACCESSION NUMBER: 1996:87548 HCAPLUS
DOCUMENT NUMBER: 124:260835
TITLE: Indole-2-carboxylic acids as nonpeptide endothelin antagonists
INVENTOR(S): Berryman, Kent A.; Bunker, Amy M.; Doherty, Annette M.; Edmunds, Jeremy J.
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: U.S., 12 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5482960	A	19960109	US 1994-339381	19941114
WO 9615125	A1	19960523	WO 1995-US12672	19951002
W: CA, EE, JP, LT, LV, MX, SI				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2202051	AA	19960523	CA 1995-2202051	19951002
EP 790993	A1	19970827	EP 1995-937320	19951002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10508843	T2	19980902	JP 1995-516037	19951002

PRIORITY APPLN. INFO.: US 1994-339381 19941114
WO 1995-US12672 19951002

OTHER SOURCE(S): MARPAT 124:260835
GI



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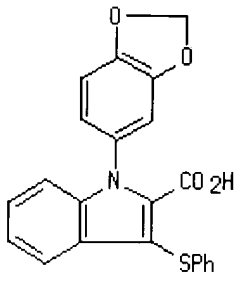
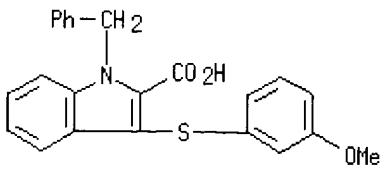


II

AB Novel indole and indoline nonpeptide antagonists I of endothelin I are described, wherein the dotted line indicates an optional bond; n is 0-4; R1 is Ph, in which the Ph group is substituted by methylenedioxy and further unsubstituted or substituted by, e.g., halo, C1-6 alkyl; R2 is, e.g., H, CO2R, tetrazolyl, R = e.g., H, C1-6 alkyl,; R3 = S(O)pPh, in which p is 0, 1, or 2 and Ph is unsubstituted or substituted by, e.g., halo, NO2, N3; R4 is one to four independent substituents selected from, e.g., hydrogen, alkyl of 1-7 carbon atoms, alkenyl of 2-7 carbon atoms, alkynyl of 2-7 carbon atom, cycloalkyl, Ph; as well as novel intermediates used in their prepn., methods for the prepn. and pharmaceutical compns. of the same, which are useful in treating elevated levels of endothelin, essential renovascular malignant and pulmonary hypertension, cerebral infarction, cerebral ischemia, congestive heart failure and subarachnoid hemorrhage. Thus, e.g., phenylsulfenylation of indole-2-carboxylic acid followed by treatment with Cu(II) oxide, 4-iodo-1,2-methylenedioxybenzene, and KOH afforded 1-(benzo[1,3]dioxol-5-yl)-3-phenylsulfanyl-1H-indole-2-carboxylic acid (II). In radioligand binding assays, the following cultured cells were used: rabbit renal artery vascular smooth muscle cells (ERBA-A), Ltk-cells expressing recombinant human ETAR (HERBA-A), and CHO-K1 cells expressing recombinant human ETBR (HERBA-B); II exhibited endothelin receptor binding activity with IC50 = 1.9, 3.2, and 6.5 μM in the ERBA-A, HERBA-A, and HERBA-B assays, resp.

IT **175339-72-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(indole-2-carboxylic acids as nonpeptide endothelin antagonists)

RN 175339-72-7 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 3-[(3-methoxyphenyl)thio]-1-(phenylmethyl)-(9CI) (CA INDEX NAME)



L14 ANSWER 24 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

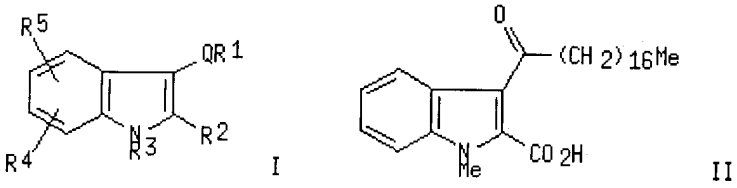
ACCESSION NUMBER: 1995:638471 HCAPLUS
DOCUMENT NUMBER: 123:32958
TITLE: Indole-2-alkanoic acids and their derivatives as

inhibitors of phospholipase A2.
INVENTOR(S): Lehr, Matthias
PATENT ASSIGNEE(S): Germany
SOURCE: Ger. Offen., 30 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4338770	A1	19950518	DE 1993-4338770	19931112
WO 9513266	A1	19950518	WO 1994-DE1121	19940920
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9476907	A1	19950529	AU 1994-76907	19940920

PRIORITY APPLN. INFO.: DE 1993-4338770 19931112
WO 1994-DE1121 19940920

OTHER SOURCE(S): MARPAT 123:32958
GI

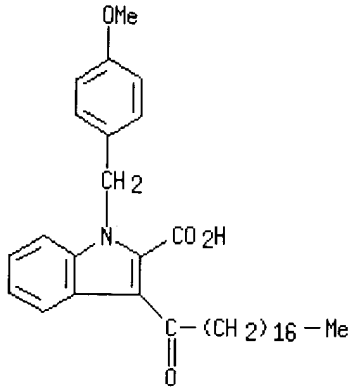


AB Title compds. I [R1 = X, (un)substituted aryl, -X-aryl; X = C1-19 alk(en/yn)yl optionally interrupted by O; R2 = CO2H, -Y-CO2H, Tz, -Y-Tz; Y = C1-8 alk(en)yl optionally interrupted by O; Tz = 1H- or 2H-tetrazol-5-yl; R3 = H, Z (Z = C1-20 alk(en/yn)yl optionally interrupted by O), (un)substituted aryl or -Z-aryl, or Z (un)substituted by OH, acyloxy, SH, acylthio, NH2, or acylamino; Q = CO, CH2, (acylamino)methylene; R4, R5 = H, as given for Z, halo, CF3, OH, cyano, many others] and their pharmaceutical salts and esters are claimed. The compds. are inhibitors of phospholipase A2 (PLA2), and are claimed useful for treatment or prevention of inflammation, allergy, asthma, psoriasis, and endotoxin shock. For example, acylation of indole-2-carboxylic acid Et ester with octadecanoic acid in CH2Cl2 in the presence of polyphosphoric acid and (CF3CO)2O gave 42% 3-octadecanoyl deriv., which was N-alkylated by p-MeC6H4SO3Me under phase-transfer conditions (75%) and hydrolyzed by aq. KOH in refluxing EtOH (80%) to give title compd. II. In a test for inhibition of PLA2 using bovine platelets in vitro, II at 10 μM gave 61% inhibition, vs. only 42% for the known inhibitor (S)-N-hexadecyl-2-pyrrolidinecarboxamide.

IT **164160-85-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of indolealkanoic acids as phospholipase A2 inhibitors)

RN 164160-85-4 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(4-methoxyphenyl)methyl]-3-(1-oxooctadecyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 25 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1995:354655 HCAPLUS
DOCUMENT NUMBER: 123:256509
TITLE: Substituted indole derivatives as angiotensin II antagonists
INVENTOR(S): Clark, Robin D.; Clarke, David E.; Fisher, Lawrence E.; Jahangir, Alam
PATENT ASSIGNEE(S): Syntex (U.S.A.) Inc., USA
SOURCE: U.S., 45 pp. Cont.-in-part of U.S. 5,212,195.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5380739	A	19950110	US 1993-4869	19930204
US 5212195	A	19930518	US 1992-882390	19920513
WO 9323391	A1	19931125	WO 1993-US1533	19930226
W: AU, CA, FI, HU, JP, KR, NO, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9337274	A1	19931213	AU 1993-37274	19930226
AU 672599	B2	19961010		
EP 640080	A1	19950301	EP 1993-906123	19930226
EP 640080	B1	19971022		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
HU 68056	A2	19950529	HU 1994-3238	19930226
JP 07506826	T2	19950727	JP 1993-520179	19930226
JP 3332234	B2	20021007		
AT 159524	E	19971115	AT 1993-906123	19930226
IL 104869	A1	19971120	IL 1993-104869	19930226
ES 2110086	T3	19980201	ES 1993-906123	19930226
CN 1039714	B	19980909	CN 1993-102401	19930226
NZ 299146	A	20000623	NZ 1993-299146	19930226
FI 9405319	A	19941111	FI 1994-5319	19941111
NO 9404311	A	19941114	NO 1994-4311	19941111

PRIORITY APPLN. INFO.:

US 1992-882390	A2	19920513
US 1993-4869	A	19930204
NZ 1993-249729	A1	19930226

WO 1993-US1533 A 19930226

OTHER SOURCE(S): MARPAT 123:256509

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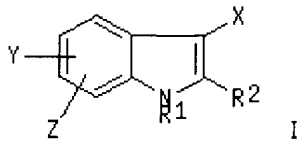


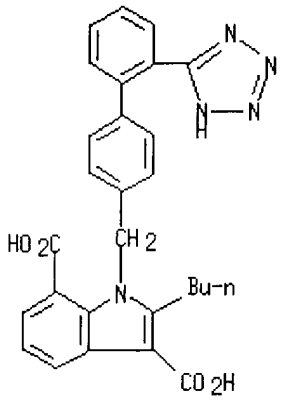
I

AB Indole derivs. I [wherein: R1 is lower alkyl, cycloalkyl, or cycloalkyl lower alkyl; R2 is 2''-(1H-tetrazol-5-yl)biphenyl-4'-ylmethyl; X is hydrogen, lower alkyl, halogen, C(O)CF3, CO2R4, or C(O)NR5R6 ; Y is hydrogen, lower alkyl, lower alkoxy, hydroxy, halogen, CO2R4 ; Z is hydrogen, lower alkyl, lower alkoxy, or halogen; wherein R4 is hydrogen or lower alkyl; R5 is hydrogen or lower alkyl; R6 is hydrogen or lower alkyl; or R5 and R6 taken together with the nitrogen to which they are attached represent a heterocycle; or a pharmaceutically acceptable salt thereof] exhibit useful pharmacol. properties, and are particularly useful as angiotensin II antagonists (no data). Thus, e.g., sapon. of Me 2-ethyl-1-[2''-(1H-tetrazol-5-yl)biphenyl-4'-ylmethyl]indole-7-carboxylate (prepn. given) in NaOH/MeOH/water afforded 2-ethyl-1-[2''-(1H-tetrazol-5-yl)biphenyl-4'-ylmethyl]indole-7-carboxylic acid. Pharmaceutical formulations were given.

IT **149652-42-6P**, 2-(n-Butyl)-1-[2"-(1H-tetrazol-5-yl)biphenyl-4'-ylmethyl]-3,7-dicarboxylic acid
RL: RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(indole derivs. as angiotensin II antagonists)

RN 149652-42-6 HCAPLUS

CN 1H-Indole-3,7-dicarboxylic acid, 2-butyl-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 26 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1994:270407 HCAPLUS

DOCUMENT NUMBER: 120:270407

TITLE: Preparation of substituted indoles and azaindoles as angiotensin II antagonists

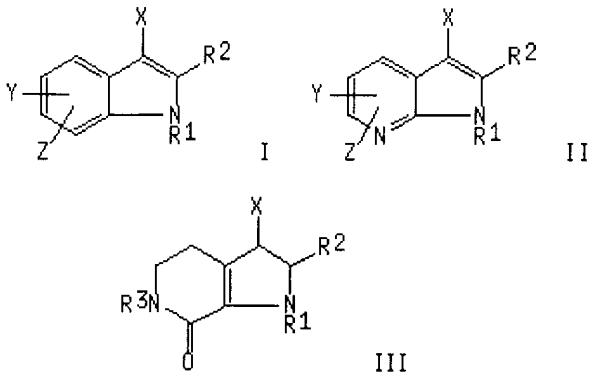
INVENTOR(S): Fisher, Lawrence E.; Clarke, David E.; Jahangir, Alam;

Clark, Robin D.
PATENT ASSIGNEE(S): Syntex (U.S.A.), Inc., USA
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9323391	A1	19931125	WO 1993-US1533	19930226
W: AU, CA, FI, HU, JP, KR, NO, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5212195	A	19930518	US 1992-882390	19920513
US 5380739	A	19950110	US 1993-4869	19930204
AU 9337274	A1	19931213	AU 1993-37274	19930226
AU 672599	B2	19961010		
EP 640080	A1	19950301	EP 1993-906123	19930226
EP 640080	B1	19971022		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07506826	T2	19950727	JP 1993-520179	19930226
JP 3332234	B2	20021007		
FI 9405319	A	19941111	FI 1994-5319	19941111
NO 9404311	A	19941114	NO 1994-4311	19941111

PRIORITY APPLN. INFO.: US 1992-882390 A 19920513
US 1993-4869 A 19930204
WO 1993-US1533 A 19930226

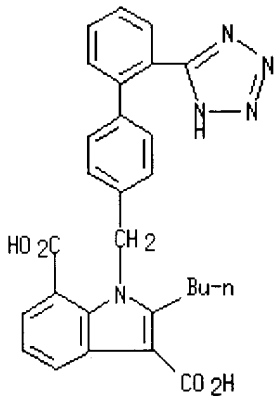
OTHER SOURCE(S): MARPAT 120:270407
GI



I II III

AB Title compds. I, II, III (R = alkyl when R2 = V, R2 = alkyl when R1 = V wherein V = R,C6H4CH2 wherein R7 = substituted Ph, substituted furanyl, substituted thiophenyl, disubstituted thiophenyl, etc.; R3 = H, alkyl; X = H, alkyl, halo, F3CCO, R4O2C wherein R4 = H, alkyl; (substituted) aminocarbonyl; Y = H, alkyl, alkoxy, HO, halo R4O2C; Z = H, alkyl, alkoxy, halo) and a salt thereof, are prepd. 1-N-butyl-2-(2-cyanobiphenyl-4-ylmethyl)indole-3-carboxylic acid (prepn. given), xylene and Bu3SuN3 were refluxed for 20 h to give I [R1 = u-Bu, R2 = 2"-(1H-tetrazol-5-yl)biphenyl-4'-ylmethyl; X = HO2C, Y = Z = H] (IV). In an assay for detn. of affinity for angiotensin II receptors the pK; of IV was 7.7. Antihypertensive activity and cognitive enhancement assay were demonstrated for the title compds. Pharmaceutical formulations of I, II and III are given.

IT **149652-42-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as angiotensin II receptor antagonist)
RN 149652-42-6 HCAPLUS
CN 1H-Indole-3,7-dicarboxylic acid, 2-butyl-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (9CI) (CA INDEX NAME)



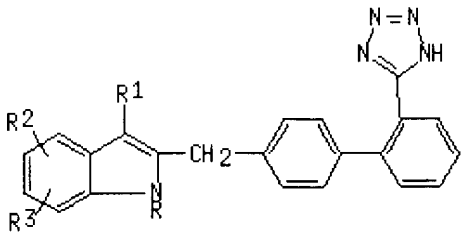
L14 ANSWER 27 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 1993:539239 HCAPLUS
DOCUMENT NUMBER: 119:139239
TITLE: Substituted indole angiotensin II antagonists
INVENTOR(S): Clark, Robin D.; Clarke, David E.; Fisher, Lawrence E.; Jahangir, Alam
PATENT ASSIGNEE(S): Syntex (U.S.A.), Inc., USA
SOURCE: U.S., 34 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5212195	A	19930518	US 1992-882390	19920513
US 5380739	A	19950110	US 1993-4869	19930204
WO 9323391	A1	19931125	WO 1993-US1533	19930226
W: AU, CA, FI, HU, JP, KR, NO, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9337274	A1	19931213	AU 1993-37274	19930226
AU 672599	B2	19961010		
ZA 9301399	A	19940826	ZA 1993-1399	19930226
EP 640080	A1	19950301	EP 1993-906123	19930226
EP 640080	B1	19971022		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
HU 68056	A2	19950529	HU 1994-3238	19930226
JP 07506826	T2	19950727	JP 1993-520179	19930226
JP 3332234	B2	20021007		
AT 159524	E	19971115	AT 1993-906123	19930226
IL 104869	A1	19971120	IL 1993-104869	19930226
ES 2110086	T3	19980201	ES 1993-906123	19930226

CN 1039714	B	19980909	CN 1993-102401		19930226
NZ 299146	A	20000623	NZ 1993-299146		19930226
FI 9405319	A	19941111	FI 1994-5319		19941111
NO 9404311	A	19941114	NO 1994-4311		19941111
PRIORITY APPLN. INFO.:			US 1992-882390	A2	19920513
			US 1993-4869	A	19930204
			NZ 1993-249729	A1	19930226
			WO 1993-US1533	A	19930226

OTHER SOURCE(S): MARPAT 119:139239
GI

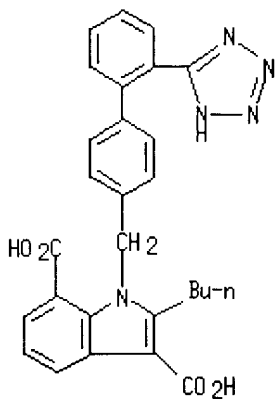


I

AB The title compds. I (R = alkyl; R1 = H, alkyl, halo, F3CCO, CO2H, alkoxycarbonyl, carbamoyl; R2 = H, alkyl, alkoxy, HO, CO2H, alkoxycarbonyl; R3 = H, allyl, alkoxy, halo) were prepd. as angiotensin II antagonists. Thus, 1-butyl-2-(2''-cyanobiphenyl-4'-ylmethyl)indole-3-carboxylic acid, prepd. in 3 steps from 2-(p-bromophenylmethyl)indole, was cyclized with tributyltin azide to give I (R = Bu, R1 = CO2H; R2 = R3 = H). The compds. were active as antagonists of angiotensin II mediated contractions of rabbit aorta and reduced blood pressure in normotensive rats (no data).

IT **149652-42-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as angiotensin II antagonist)

RN 149652-42-6 HCAPLUS
CN 1H-Indole-3,7-dicarboxylic acid, 2-butyl-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 28 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

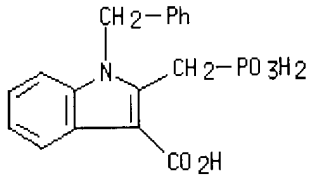
ACCESSION NUMBER: 1992:462319 HCAPLUS
DOCUMENT NUMBER: 117:62319

TITLE: Synthesis and biological evaluation of some new phosphonates
AUTHOR(S): Garuti, I.; Ferranti, A.; Roberti, M.; Katz, E.; Budriesi, R.; Chiarini, A.
CORPORATE SOURCE: Dep. Pharm. Sci., Univ. Bologna, Bologna, Italy
SOURCE: Pharmazie (1992), 47(4), 295-7
CODEN: PHARAT; ISSN: 0031-7144
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A group of 21 aryl phosphonates [(HO)2P(O)CH2XCO2H, X = aryl] was prepd. from the corresponding methylarylcarboxylic acids or their Et esters, which were then converted to bromomethyl derivs. These were reacted directly with tri-Et phosphite (Michaelis Arbuzov reaction) and the crude products obtained were hydrolyzed with 6M HCl to yield the desired compds. They were screened for cytotoxicity, antiviral activity, as antagonists at various excitatory amino acid receptors, for chronotropic and inotropic effects, and for Ca2+-antagonist activity. Only their neg. inotropic properties appeared to merit further investigation.

IT **142646-23-9P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(prepn. and pharmacol. of)

RN 142646-23-9 HCAPLUS
CN 1H-Indole-3-carboxylic acid, 1-(phenylmethyl)-2-(phosphonomethyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 29 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

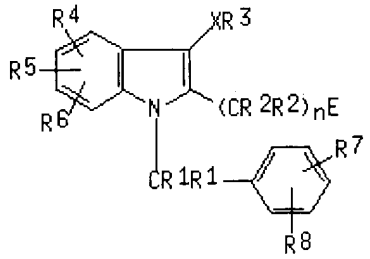
ACCESSION NUMBER: 1992:255478 HCAPLUS
DOCUMENT NUMBER: 116:255478
TITLE: Preparation of 3-alkylthio-N-benzylindoles and related compounds as leukotriene inhibitors
INVENTOR(S): Gillard, John W.; Morton, Howard E.; Fortin, Rejean; Guindon, Yvan
PATENT ASSIGNEE(S): Merck Frosst Canada Inc., Can.
SOURCE: U.S., 30 pp. Cont.-in-part of U.S. Ser. No. 942,900, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5081138	A	19920114	US 1987-130771	19871209
CA 1334415	A1	19950214	CA 1987-553922	19871209
US 5225421	A	19930706	US 1991-760443	19910916

PRIORITY APPLN. INFO.: US 1986-942900 19861217
US 1987-130771 19871209

OTHER SOURCE(S): MARPAT 116:255478

GI



I

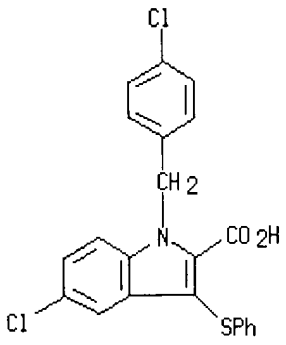
AB Title compds. I [R1, R2 = H, C1-7 alkyl; CR2R2 = 3-6 membered ring; R3 = (substituted) C1-20 alkyl, C2-6 alkenyl, (substituted) Ph, (CH2)mHet; R4-R6 = H, C1-7 alkyl, C2-6 alkenyl, (CR2R2)pM; R7, R8 = H, C1-3 alkyl, halo, OH, cyano, CF3, C1-3 alkoxy, C1-3 alkylthio, CO2H, C1-3 alkoxycarbonyl, C1-3 alkylcarbonyl, N3; R9 = CF3, C1-7 alkyl, (substituted) benzyl, (substituted) Ph; R10 = H, C1-7 alkyl, Ph, CH2Ph; NR10R10 = 5-7 membered ring; R11 = H, (CH2)qR9; R13 = H, C1-7 alkyl, (substituted) Ph, (substituted) benzyl; R14 = CH2CH2N(R10)2, CH2CHOHCH2OH, CH2O2CCMe3, CHMeO2CCMe, etc.; E = CH2OH, CO2R13, CO2R14, tetrazol-5-yl, CHO, CONR2R2, CONHSO2R9, CON(OR2)R2; M = OR10, halo, CF3, SR7, (substituted) Ph, CO2R10, COR11, tetrazolyl, etc.; X = O, S, SO, SO2, Het = pyridyl, tetrazolyl, thienyl, thiazolyl, etc.; m = 0-2; n = 0-5; p = 0-3; q = 0-4] were prepd. as leukotriene inhibitors useful as antiasthmatics, antiallergics, antiinflammatories, and cytoprotective agents (no data). Thus, 1-p-chlorobenzyl-1-(4-fluorophenyl)hydrazine.HCl was added to Et 4-methylthio-3-oxobutanoate in Me3COH and the mixt. was refluxed under N for 16 h to give title compd. I [R1, R2, R5-R7 = H; R3 = Me; R4 = 5-F; R8 = 4-Cl; n = 1; E = CO2Et; X = S].

IT **118414-59-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as leukotriene inhibitor)

RN 118414-59-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 5-chloro-1-[(4-chlorophenyl)methyl]-3-(phenylthio)- (9CI) (CA INDEX NAME)



L14 ANSWER 30 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1989:573982 HCAPLUS
Correction of: 1987:213760
DOCUMENT NUMBER: 111:173982
Correction of: 106:213760
TITLE: Acidic indole compounds and their use as antiallergy agents
INVENTOR(S): Connor, David T.; Unangst, Paul C.; Stabler, S. Russell
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: Eur. Pat. Appl., 60 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 186367	A2	19860702	EP 1985-308948	19851210
EP 186367	A3	19880107		
EP 186367	B1	19930303		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4675332	A	19870623	US 1985-788111	19851021
ZA 8508651	A	19870624	ZA 1985-8651	19851111
AU 8550508	A1	19860619	AU 1985-50508	19851129
AU 576131	B2	19880811		
FI 8504821	A	19860611	FI 1985-4821	19851204
FI 84719	B	19910930		
FI 84719	C	19920110		
DK 8505688	A	19860611	DK 1985-5688	19851209
DK 174104	B1	20020617		
NO 8504941	A	19860611	NO 1985-4941	19851209
NO 159653	B	19881017		
NO 159653	C	19890125		
JP 61191683	A2	19860826	JP 1985-275227	19851209
JP 06053736	B4	19940720		
ES 549768	A1	19860416	ES 1985-549768	19851210
CN 85109061	A	19870121	CN 1985-109061	19851210
CN 1005974	B	19891206		
CA 1259317	A1	19890912	CA 1985-497268	19851210
AT 86252	E	19930315	AT 1985-308948	19851210

PRIORITY APPLN. INFO.:
US 1984-680116 A 19841210
US 1985-788111 A 19851021
EP 1985-308948 A 19851210

OTHER SOURCE(S): CASREACT 111:173982
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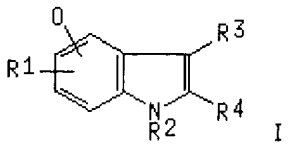


I

AB The title compds. [I; R1, Q = H, C1-12 alkyl, alkoxy, SH, C1-4 alkylthio, alkylsulfinyl, OH, NO2, halo, (un)substituted NH2; R1Q = OCH2O; R2 = H, C1-12 alkyl, (un)substituted Ph, PhCH2; R3 = H, C1-12 alkyl, alkoxy, etc.; R4 = tetrazolyl, tetrazolylcarbamoyl] and their salts, useful as antiallegic agents (no data) were prepd. Thus, 3-methoxy-1-(phenylmethyl)-1H-indole-2-carboxylic acid, prepd. by N-benzylation of Et

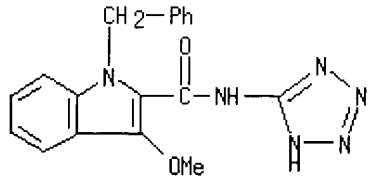
3-methoxy-1H-indole-2-carboxylate followed by sapon., was amidated with 5-aminotetrazole in the presence of 1,1'-carbonyldiimidazole in DMF to give 3-methoxy-1-(phenylmethyl)-N-1H-tetrazol-5-yl-1H-indole-2-carboxamide.

IT **104961-18-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as antiallergic agent)

RN 104961-18-4 HCAPLUS

CN 1H-Indole-2-carboxamide, 3-methoxy-1-(phenylmethyl)-N-1H-tetrazol-5-yl- (9CI) (CA INDEX NAME)



L14 ANSWER 31 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

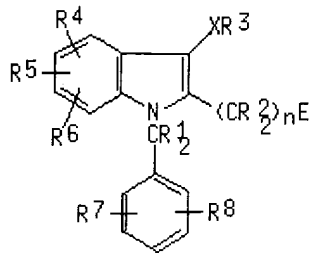
Full Text | Citing References

ACCESSION NUMBER: 1989:57508 HCAPLUS
DOCUMENT NUMBER: 110:57508
TITLE: Preparation and formulation of 3-hetero-substituted-N-benzyl-indoles as inhibitors of leukotriene biosynthesis
INVENTOR(S): Gillard, John W.; Morton, Howard E.; Fortin, Rejean; Guindon, Yvan
PATENT ASSIGNEE(S): Merck Frosst Canada, Inc., Can.
SOURCE: Eur. Pat. Appl., 78 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 275667	A1	19880727	EP 1987-311031	19871215
EP 275667	B1	19920318		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
IL 84796	A1	19920329	IL 1987-84796	19871211
ZA 8709401	A	19880727	ZA 1987-9401	19871215
AT 73770	E	19920415	AT 1987-311031	19871215
AU 8782603	A1	19880623	AU 1987-82603	19871216
AU 603402	B2	19901115		
DK 8706608	A	19880925	DK 1987-6608	19871216
JP 63246372	A2	19881013	JP 1987-317663	19871217

PRIORITY APPLN. INFO.: CA 1986-525670 19861217
EP 1987-311031 19871215

OTHER SOURCE(S): MARPAT 110:57508
GI



I

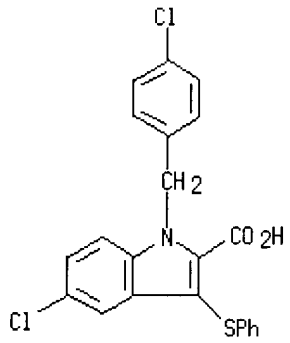
AB Title compds. I [R1 = H, alkyl; R2 = H, alkyl, R22 = C3-6 ring; R3 = alkyl, C3-6 alkenyl, (un)substituted Ph, R(CH2)m, M-substituted alkyl; R = heterocyclyl; m = 0-2; M = halo, F3C, F3CS, (un)substituted Ph, tetrazole, O2N, H, etc.; R4, R5, R6 = H, alkyl; C2-6 alkenyl, etc; R7, R8 = H, C1-3 alkyl, halo, HO, cyano, F3C, C1-3 alkoxy, C1-3 alkylthio, HO2C, C1-3 alkoxycarbonyl, C1-3 alkylcarbonyl, N3; E = HOCH2, HO2C, alkyl-O2C, (un) substituted PhO2C, tetrazol-5-yl, HCO, HOCH2CH(OH)CH2O2C, etc.; X = O, S, SO, SO2; n = 0-5] and their pharmaceutically acceptable salts, useful as inhibitors of leukotriene biosynthesis (no data), were prepd. To Et 5-chloro-3-(phenylthio)indole-2-carboxylate in THF was added K hexamethylsilamide in PhMe, followed by 4-ClC6H4CH2Cl, Hempa and Bu4NBr to give I (R1, R5, R6, R8 = H; R3 = Ph; R4 = 5-Cl; R1 = 4-Cl; n = 0; E = EtO2C).

IT **118414-59-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as leukotriene biosynthesis inhibitor)

RN 118414-59-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 5-chloro-1-[(4-chlorophenyl)methyl]-3-(phenylthio)- (9CI) (CA INDEX NAME)



L14 ANSWER 32 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

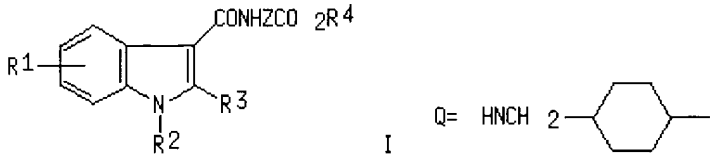
Full Text | Citing References

ACCESSION NUMBER:	1988:94380 HCAPLUS
DOCUMENT NUMBER:	108:94380
TITLE:	Preparation of 3-indolecarboxamide derivatives as analgesics, inflammation inhibitors and 5-lipoxygenase inhibitors
INVENTOR(S):	Nakao, Tatsu; Saito, Tadamasa; Terasawa, Michio; Tawara, Tetsuji
PATENT ASSIGNEE(S):	Yoshitomi Pharmaceutical Industries, Ltd., Japan
SOURCE:	Jpn. Kokai Tokkyo Koho, 6 pp. CODEN: JKXXAF
DOCUMENT TYPE:	Patent

LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 62138469	A2	19870622	JP 1985-278472	19851211

PRIORITY APPLN. INFO.: JP 1985-278472 19851211
GI

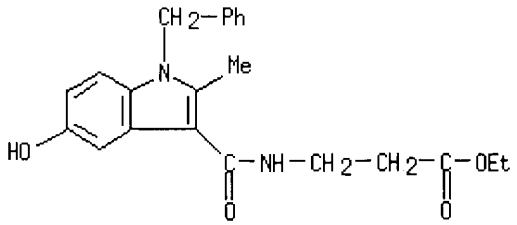


I

AB The title compds. [I; R1 = H, halo, OH, alkanoyl; R2 = H, alkyl, (substituted) Ph, aralkyl; R3 = alkyl; R4 = H, alkyl; Z = C1-6 alkylene, cyclohexylenemethyl, phenylene], useful as analgesics, antiinflammatory agents, and 5-lipoxygenase inhibitors, are prepd. Treatment of 5-hydroxy-2-methylindole-3-carboxylic acid and Et trans-4-aminoethylcyclohexane-1-carboxylate.HCl in THF with 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide in the presence of Et3N gave I (R1 = 5-OH; R2 = H; R3 = Me; R4 = Et; Z = trans-Q). I (R1 = 5-OH; R2 = PhCH2; R3 = Me; R4 = Et; Z = trans-Q) at 100 mg/kg p.o. showed 62% analgesic activity in rats treated with phenylquinone i.p.

IT **113077-88-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as analgesic, antiinflammatory agent, and lipoxygenase inhibitor)

RN 113077-88-6 HCAPLUS
CN β-Alanine, N-[[5-hydroxy-2-methyl-1-(phenylmethyl)-1H-indol-3-yl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 33 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1988:21703 HCAPLUS
DOCUMENT NUMBER: 108:21703
TITLE: Preparation of heterocyclic enol amide derivatives as pharmaceuticals
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 78 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 62081369	A2	19870414	JP 1986-230231	19860930
US 4761424	A	19880802	US 1985-782623	19851001
ZA 8606973	A	19880427	ZA 1986-6973	19860912
AU 8663285	A1	19870402	AU 1986-63285	19860929
AU 605747	B2	19910124		
DK 8604664	A	19870406	DK 1986-4664	19860930
EP 221345	A1	19870513	EP 1986-113489	19861001
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ES 2002398	A6	19880801	ES 1986-2338	19861001
US 4921871	A	19900501	US 1987-121264	19871116
US 4874758	A	19891017	US 1988-164355	19880304
US 4868195	A	19890919	US 1988-165045	19880307
US 4868199	A	19890919	US 1988-167264	19880309
US 4868200	A	19890919	US 1988-166146	19880309
US 4868205	A	19890919	US 1988-167272	19880311

PRIORITY APPLN. INFO.: US 1985-782623 19851001
US 1987-121264 19871116

OTHER SOURCE(S): CASREACT 108:21703
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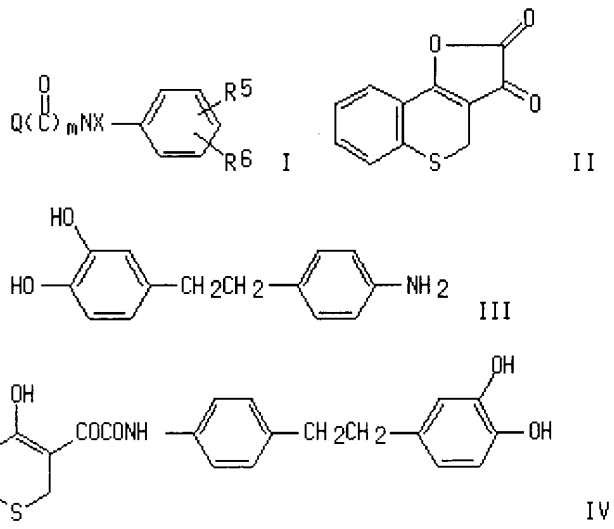
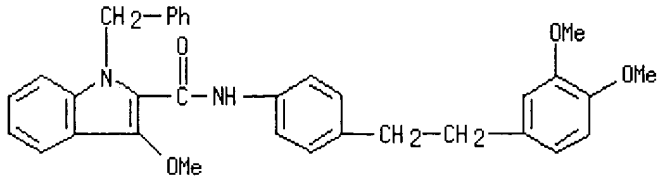


AB The title compds. (I; Q = benzofuryl, benzothienyl, indolyl, benzopyranyl, benzothiopyranyl, etc.; R5 = H, C1-4 alkyl, alkoxy, C2-4 carbalkoxy, etc.; R6 = C6-20 alkyl, styryl, etc.; X = H, alkyl; m = 1, 2), useful as pharmaceuticals, are prepd. A mixt. of 0.085 mol furandione deriv. II and 0.0749 mol aniline deriv. III in THF was stirred at room temp. under N, the solvent distd. in vacuo, and the solid product was refluxed in CH2Cl2 to give 85.2% enol amide IV. I showed ID50 against 5-lipoxygenase at 1.06-9.30M.

IT **111926-88-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as drug)

RN 111926-88-6 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[4-[2-(3,4-dimethoxyphenyl)ethyl]phenyl]-3-methoxy-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	282.84	601.45

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-38.12	-38.12

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FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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L3 514 S L1 FULL
L4 STRUCTURE UPLOADED
L5 0 S L4
L6 0 S L4 FULL

FILE 'HCAPLUS' ENTERED AT 15:02:52 ON 15 JUN 2004
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L8 18 S L7 AND INFLAMM?
L9 3 S L8 AND FAULL, A?/AU
L10 4 S L7 AND FAULL, A?/AU
L11 3 S L8 AND KETTLE, J?/AU

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L12             4 S L7 AND KETTLE, J?/AU
L13             0 S L12 NOT L10
L14            33 S L7 NOT L12

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=> s l3
L15             7 L3

=> s l15 and inflamm?
          1978 INFLAMM?
L16             0 L15 AND INFLAMM?

=> d l15, all, 1-7

L15  ANSWER 1 OF 7  CAOLD  COPYRIGHT 2004 ACS on STN
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Full Text

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AN   CA65:3843e  CAOLD
TI   7-(diphenylmethyl)-7-hydroxy-2,3-norbornane-dicarboxylic acid
     γ-lactones (isomeric)
PA   McNeil Laboratories, Inc.
DT   Patent
TI   isomeric 7-(diphenylmethyl)-7-hydroxy-2,3-norbornanedicarboxylic acid
     γ-lactones
AU   Poos, George I.
DT   Patent
TI   α-(1-benzyl-3-indolyl)alkanecarboxylic acids
AU   Sarett, Lewis H.; Shen, T. Y.
PA   Merck & Co., Inc.
DT   Patent
     PATENT NO.     KIND          DATE
     ------------   -----------   ----
PI   US 3242163                   1966
     NL 6513089
PI   US 3250789                   1966
IT    349-95-1     455-19-6     874-87-3     939-99-1    1129-01-7    1140-46-1
     1140-47-2    1208-87-3    1583-83-1    1703-96-4    1959-23-5    1995-51-3
     2175-90-8    2320-32-3    3446-61-5    3446-65-9    3446-67-1   3446-68-2
     3446-69-3    3446-75-1    3446-77-3    3446-79-5    3446-80-8    3446-81-9
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     3447-16-3    3447-17-4    3447-18-5    3447-19-6    3447-20-9    3447-21-0
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6715-60-2 6724-58-9 6827-79-8 7199-52-2 7200-75-1 13858-02-1
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95822-68-7 96309-57-8 96367-30-5 96467-96-8 96585-34-1 96761-91-0
97152-77-7 97257-35-7 101316-92-1 101698-87-7 101918-24-5 102130-47-2
102263-44-5 102602-92-6 106249-10-9 106524-27-0

L15 ANSWER 2 OF 7 CAOLD COPYRIGHT 2004 ACS on STN

Full Text

AN CA65:3840e CAOLD

TI α-(1-benzyl-3-indolyl)alkanecarboxylic acids

AU Sarett, Lewis H.; Shen, T. Y.

PA Merck & Co., Inc.

DT Patent

PATENT NO.	KIND	DATE
US 3242193		1966

IT 349-95-1 455-19-6 874-87-3 939-99-1 1129-01-7 1140-46-1
1140-47-2 1208-87-3 1568-47-4 1583-83-1 1703-96-4 1959-23-5
1995-51-3 3446-61-5 3446-65-9 3446-67-1 **3446-68-2** **3446-69-3**
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3875-69-2 4556-90-5 6211-92-3 6260-39-5 6260-74-8 6644-59-3
6644-65-1 6715-60-2 6768-99-6 6769-00-2 6769-01-3 6827-79-8
95291-44-4 97254-55-2 97254-56-3 102602-92-6 106524-27-0

L15 ANSWER 3 OF 7 CAOLD COPYRIGHT 2004 ACS on STN

Full Text

AN CA65:688d CAOLD

TI indolyl aliphatic acids

AU Sarett, Lewis H.; Shen, T. Y.

PA Merck & Co., Inc.

DT Patent

PATENT NO.	KIND	DATE
US 3242162		1966

IT 349-95-1 455-19-6 622-38-8 874-87-3 939-99-1 1129-01-7
1140-46-1 1140-47-2 1208-87-3 1568-47-4 1583-83-1 1959-23-5
3446-65-9 3446-67-1 **3446-68-2** **3446-69-3** 3446-75-1 3446-77-3
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3447-41-4 3447-44-7 3447-46-9 3447-50-5 3447-51-6 3447-53-8
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3721-31-1 3721-33-3 3721-34-4 3875-69-2 4556-90-5 4648-25-3
6211-92-3 6260-37-3 6260-39-5 6260-41-9 6260-66-8 6260-95-3
6514-35-8 6514-89-2 **6825-11-2** 95291-44-4 102603-08-7 106524-27-0

L15 ANSWER 4 OF 7 CAOLD COPYRIGHT 2004 ACS on STN

Full Text

AN CA64:8139d CAOLD
TI basic indole-3-carboxylic acid esters and amides
PA Byk-Gulden Lomberg, Chemische Fabrik G.m.b.H.
DT Patent

PATENT NO.	KIND	DATE
FR M3604		
GB 1045988		
NL 302983		
JP 65018118		1965
US 3230234		1966

IT **5091-11-2** **5091-12-3** **5091-13-4** **5091-14-5** **5091-15-6**
5091-16-7 5091-17-8 5091-30-5 5091-31-6 5091-32-7 5091-33-8
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5091-40-7 5091-59-8 5091-60-1 5091-61-2 5091-62-3 5091-63-4
5091-64-5 5091-72-5 5091-73-6 5091-74-7 5091-75-8 **5091-76-9**
5195-48-2 5195-49-3 5564-31-8 5564-32-9 5564-33-0 5564-34-1

L15 ANSWER 5 OF 7 CAOLD COPYRIGHT 2004 ACS on STN

Full Text

AN CA63:16309f CAOLD
TI indoledicarboxylic acids
PA Fujisawa Pharmaceutical Co., Ltd.
DT Patent

PATENT NO.	KIND	DATE
JP 65019336		1965

IT 3606-50-6 3606-51-7 3606-52-8 **3606-53-9**

L15 ANSWER 6 OF 7 CAOLD COPYRIGHT 2004 ACS on STN

Full Text

AN CA63:16308a CAOLD
TI indolyl aliphatic acids
AU Sarett, Lewis H.; Shen, T. Y.
PA Merck & Co., Inc.
DT Patent

PATENT NO.	KIND	DATE
US 3196162		1965

IT 349-95-1 455-19-6 622-38-8 874-87-3 939-99-1 1129-01-7
1140-46-1 1140-47-2 1208-87-3 1568-47-4 1583-83-1 1703-96-4
1959-23-5 1995-51-3 3446-67-1 **3446-68-2** **3446-69-3** 3446-72-8
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4753-18-8 23887-48-1 95291-44-4

L15 ANSWER 7 OF 7 CAOLD COPYRIGHT 2004 ACS on STN
AN CA55:2610a CAOLD
TI substituted 5-hydroxyindoles - (I) N-substituted 1-benzyl-2-methyl-3-amino-methyl-5-methoxyindoles and related compds.
AU Domschke, Guenter; Fuerst, H.
IT 18152-59-5 59513-85-8 63746-08-7 **77294-34-9** 94067-26-2 97391-70-3
101202-17-9 101735-60-8 **102081-27-6** 102552-32-9 102654-84-2 102667-11-8
102747-63-7 **102749-87-1** 102759-77-3 102810-12-8 **102892-41-1**
103326-08-5 **103329-34-6** **109254-20-8** **109254-21-9** **109559-12-8**
109814-03-1 112351-63-0 **112819-63-3** 115036-63-0 118801-30-2 120548-84-7
122765-71-3 124106-07-6 **132105-71-6** **132105-72-7**

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L8 ANSWER 1 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

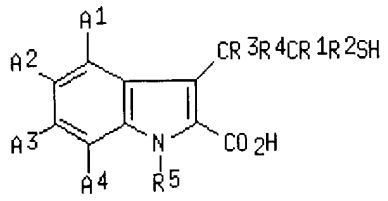
ACCESSION NUMBER: 2003:551494 HCAPLUS
DOCUMENT NUMBER: 139:101027
TITLE: Preparation of mercaptoethyl indolecarboxylic acids as NAALAdase inhibitors for treating and diagnosing glutamate abnormalities, neurological and other disorders
INVENTOR(S): Tsukamoto, Takashi; Grella, Brian; Majer, Pavel
PATENT ASSIGNEE(S): Guilford Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057670	A2	20030717	WO 2002-US37617	20021219
WO 2003057670	A3	20031106		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-342764P P 20011228
OTHER SOURCE(S): MARPAT 139:101027
GI



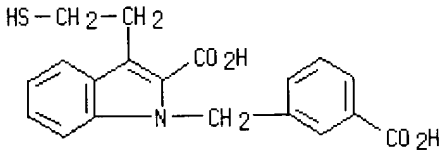
I

AB This invention relates to new indoles (shown as I; variables defined below; e.g. 3-(2-mercaptoethyl)-1H-indole-2-carboxylic acid), pharmaceutical compns. and diagnostic kits comprising such compds., and methods of using such compds. for inhibiting NAALADase enzyme activity, detecting diseases where NAALAdase levels are altered, affecting neuronal activity, effecting TGF-β activity, inhibiting angiogenesis, and treating glutamate abnormalities, neuropathy, pain, compulsive disorders, prostate diseases, cancers and glaucoma. IC50 values are tabulated for inhibition of NAALAdase by 12 examples of I. Many pharmacol. and therapeutic test results are reported for the following 6 compds. that are

not covered by I: 2-[[(2,3,4,5,6-pentafluorobenzyl)hydroxyphosphinyl]methyl]pentanedioic acid, 2-(3-sulfanylpropyl)pentanedioic acid, 2-(phosphonomethyl)pentanedioic acid, 2-(2-sulfanylethyl)pentanedioic acid, 3-carboxy-α-(3-mercaptopropyl)benzenepropanoic acid and 3-carboxy-5-(1,1-dimethylethyl)-α-(3-mercaptopropyl)benzenepropanoic acid. For I: A1, A2, A3 and A4 = H, C1-C9 alkyl, C2-C9 alkenyl, C2-C9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, C1-C9 alkoxy, C2-C9 alkenyloxy, phenoxy, benzyloxy, hydroxy, halo, nitro, cyano, isocyano, -COOR6, - COR6, -NR6R7, -SR6, -SOR6, -SO2R6, -SO2(OR6), -C(O)NR6R7, -C(O)NR6 (CH2)nCOOH, -NR6C(O)R7 or -(CH2)nCOOH, or any adjacent two of A1, A2, A3 and A4 form with the benzene ring a fused ring that is (un)satd., arom. or nonarom., and carbocyclic or heterocyclic, said heterocyclic ring contg. 1 or 2 O, N and/or S heteroatom(s); n is 1-3; R, R1, R2, R3, R4, R5, R6, R7 = H, carboxy, C1-C9 alkyl, C2-C9 alkenyl, C2-C9 alkynyl, aryl, heteroaryl, carbocycle or heterocycle; and said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenyloxy, phenoxy, benzyloxy and fused ring (un)substituted with ≥1 substituent(s). Although the methods of prepn. are not claimed, 13 example prepns. are included.

IT **560131-44-4P**, 1-[(3-Carboxyphenyl)methyl]-3-(2-mercaptoethyl)-1H-indole-2-carboxylic acid
RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate and diagnosis agent; prepn. of mercaptoethyl indolecarboxylic acids as NAALAdase inhibitors for treating and diagnosing glutamate abnormalities and neurol. and other disorders)

RN 560131-44-4 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(3-carboxyphenyl)methyl]-3-(2-mercaptoethyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 2 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

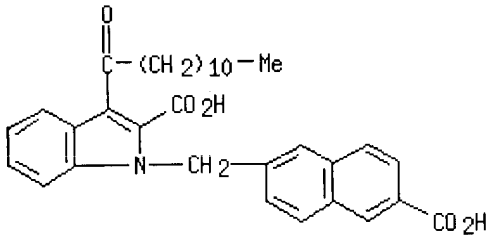
ACCESSION NUMBER:	2003:221341 HCAPLUS
DOCUMENT NUMBER:	139:111060
TITLE:	Structure-activity relationship studies of 1-substituted 3-dodecanoylindole-2-carboxylic acids as inhibitors of cytosolic phospholipase A2-mediated arachidonic acid release in intact platelets
AUTHOR(S):	Griessbach, Klaus; Klimt, Monika; Elfringhoff, Alwine Schulze; Lehr, Matthias
CORPORATE SOURCE:	Institute of Pharmaceutical and Medicinal Chemistry, University of Munster, Munster, D-48149, Germany
SOURCE:	Archiv der Pharmazie (Weinheim, Germany) (2003), Volume Date 2002, 335(11-12), 547-555 CODEN: ARPMAS; ISSN: 0365-6233
PUBLISHER:	Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 139:111060

AB A series of 3-dodecanoylindole-2-carboxylic acid derivs. with varied

carboxylic acid substituents at the indole 1-position were synthesized and evaluated for their ability to inhibit arachidonic acid release in human platelets mediated by the cytosolic phospholipase A2. Structure-activity relationship studies revealed that increasing the polarity of these substituents by the introduction of addnl. polar groups in the proximity of the carboxylic acid moiety reduced activity. Conformational restriction of the indole-1-carboxylic acid substituents in distinct positions as well as extending the length of these residues led to compds. which did not substantially differ in their potencies.

IT **562813-01-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(3-dodecanoylindole-2-carboxylic acid derivs. as cytosolic phospholipase A2 inhibitors and anti-**inflammatory** agents)

RN 562813-01-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(6-carboxy-2-naphthalenyl)methyl]-3-(1-oxododecyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

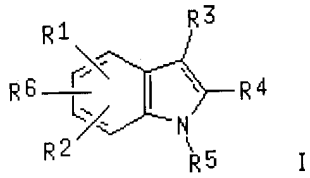
Full Text | Citing References

ACCESSION NUMBER: 2003:1275 HCAPLUS
DOCUMENT NUMBER: 138:55866
TITLE: Preparation of indole derivatives as phospholipase enzyme inhibitors for treatment of **inflammatory** conditions
INVENTOR(S): Seehra, Jasbir S.; McKew, John C.; Lovering, Frank; Bemis, Jean E.; Xiang, Yibin; Chen, Lihren; Knopf, John L.
PATENT ASSIGNEE(S): Genetics Institute, LLC, USA
SOURCE: U.S., 57 pp., Cont.-in-part of U. S. Ser. No. 256,062, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

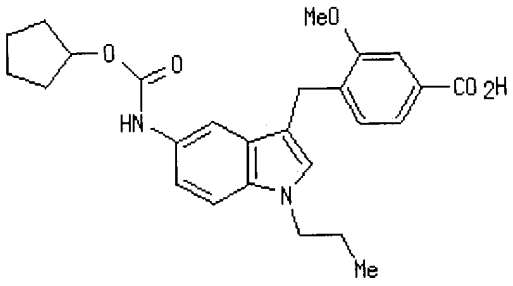
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6500853	B1	20021231	US 2000-686616	20001011

PRIORITY APPLN. INFO.: US 1998-113674P P 19980228
US 1999-256062 B2 19990224

OTHER SOURCE(S): MARPAT 138:55866
GI



I



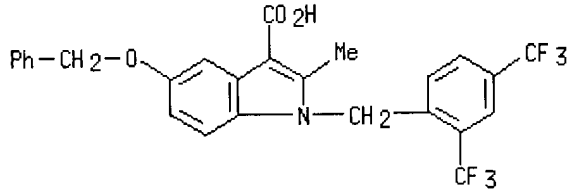
II

AB Title compds. I [wherein R1 and R6 = independently H, halo, CF3, alkyl, alkylthio, alkoxy, CN, NO2, NH2, Ph, OPh, SPh, CH2Ph, OCH2Ph, SCH2Ph, or (un)substituted amido, carbamido, sulfonyl, etc.; R2 = H, halo, CF3, OH, alkyl, alkoxy, CHO, CN, NO2, (un)substituted amino, or alkylsulfonyl; R3 = CO2H, OPO3H2, SO3H, etc.; R4 = H, CF3, alkyl, alkoxy, (alkyl)cycloalkyl, CHO, halo, etc.; R5 = alkyl, alkoxy, (alkyl)cycloalkyl, etc.; and pharmaceutically acceptable salts thereof] were prepd. as phospholipase enzyme inhibitors. For example, 5-nitroindole was C3-alkylated (55%) with Me 4-(bromomethyl)-3-methoxybenzoate in dioxane, N-alkylated (57%) with 1-iodopropane in a soln. of THF and NaH, and converted to the amine (80%) by hydrogenation using Pt/C. The amine was converted to the carbamate (39%) by addn. of cyclopentyl chloroformate in CH2Cl2 and 4-methylmorpholine, and the resultant ester was hydrolyzed to yield II (71%). The latter inhibited cytosolic phospholipase A2 (cPLA2) by 50% at a concn. of 170 μM in a coumarin assay and reduced footpad vol. by 16.61% at a dose of 5 mg/Kg IV in a carrageenan-induced footpad edema test on rats. Thus, I are useful for treatment of **inflammatory** conditions, such as arthritis, **inflammatory** bowel disease, and asthma (no data).

IT **241497-82-5P**, 1H-Indole-3-carboxylic acid, 1-[[2,4-bis(trifluoromethyl)phenyl]methyl]-2-methyl-5-(phenylmethoxy)-
RL: PAC (Pharmacological activity); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(phospholipase inhibitor; prepn. of indole derivs. as phospholipase enzyme inhibitors for treatment of **inflammatory** conditions)

RN 241497-82-5 HCAPLUS

CN 1H-Indole-3-carboxylic acid, 1-[[2,4-bis(trifluoromethyl)phenyl]methyl]-2-methyl-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:964145 HCAPLUS
DOCUMENT NUMBER: 138:19491
TITLE: A method for treating **inflammatory** diseases by administering a PPAR-δ agonist
INVENTOR(S): Forrest, Michael J.; Berger, Joel P.; Moller, David E.; Wright, Samuel
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

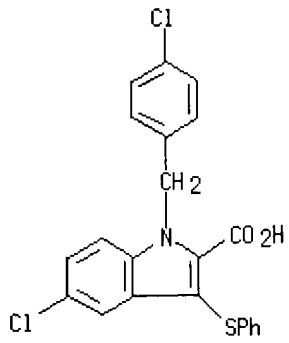
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002100351	A2	20021219	WO 2002-US20974	20020607
WO 2002100351	A3	20030501		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1399151	A2	20040324	EP 2002-746824	20020607
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2001-297356P P 20010611
WO 2002-US20974 W 20020607

AB A method for treating, controlling, preventing or reducing the risk of contracting an **inflammatory** disease or condition in a mammalian patient, comprises (1) selecting a patient in need thereof, and (2) treating the patient with a therapeutically effective amt. of a compn. comprising a PPAR-δ agonist. **Inflammatory** diseases that may be treated by this method include but are not limited to rheumatoid arthritis, juvenile rheumatoid arthritis, systemic lupus erythematosus, osteoarthritis, degenerative joint disease, one or more connective tissue diseases, ankylosing spondylitis, and bursitis.

IT **118414-59-8**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(PPAR-δ agonist for treating **inflammatory** disease, and use with other agents)

RN 118414-59-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 5-chloro-1-[(4-chlorophenyl)methyl]-3-(phenylthio)- (9CI) (CA INDEX NAME)



L8 ANSWER 5 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

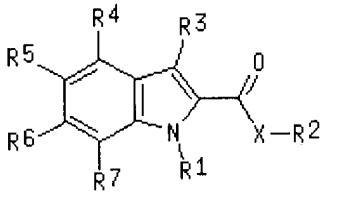
ACCESSION NUMBER: 2002:293620 HCAPLUS
DOCUMENT NUMBER: 136:309846
TITLE: Preparation of substituted indoles as PPAR-γ binding agents
INVENTOR(S): Stolle, Andreas; Dumas, Jacques P.; Carley, William; Coish, Phillip D. G.; Magnuson, Steven R.; Wang, Yamin; Nagarathnam, Dhanapalan; Lowe, Derek B.; Su, Ning; Bullock, William H.; Campbell, Ann-Marie; Qi, Ning; Baryza, Jeremy L.; Cook, James H.
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 233 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PO = Date reported

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030895	A1	20020418	WO 2001-US42644	20011009
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002011901	A5	20020422	AU 2002-11901	20011009
US 2003087902	A1	20030508	US 2001-974319	20011009
EP 1341761	A1	20030910	EP 2001-979996	20011009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2003001619	A	20030602	NO 2003-1619	20030409

PRIORITY APPLN. INFO.:
US 2000-239195P P 20001010
US 2000-243665P P 20001027
WO 2001-US42644 W 20011009

OTHER SOURCE(S): MARPAT 136:309846
GI



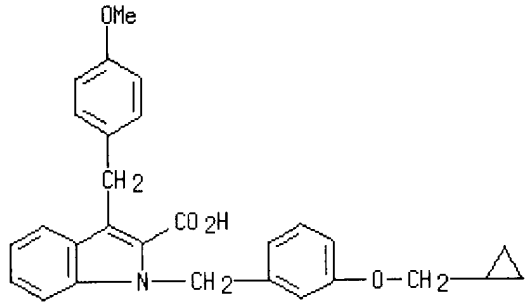
I

AB The title compds. [I; R1 = R8R9; R8 = alkyl, alkenyl, alkynyl, etc.; R9 = (un)substituted Ph, cycloalkyl, heterocycloalkyl, etc.; X = (un)substituted NH, S, O; R2 = H, alkyl, halo, alkyl, etc.; R3 = R12R13; R12 = alkyl, alkenyl, alkynyl, CO; R13 = (un)substituted cycloalkyl, cycloalkenyl, heterocycloalkyl, etc.; R4-R7 = H, OH, etc.], useful in treating or preventing PPAR-γ mediated diseases or conditions, such as osteopenia, osteoporosis, cancer, diabetes and atherosclerosis, were prepd. Thus, hydrolysis of Et 3-(cyclopropylidenemethyl)-1-[3-(trifluoromethyl)benzyl]-1H-indole-2-carboxylate (prepn. given) with NaOH in H2O/THF afforded 57% I [R1 = 3-F3CC6H4CH2; X = O; R2 = H; R3 = cyclopropylidenemethyl; R4-R7 = H] which showed IC50 of 100 pM and 9.99 nM against PPAR-γ binding.

IT **412004-67-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted indoles as PPAR-γ binding agents)

RN 412004-67-2 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[[3-(cyclopropylmethoxy)phenyl]methyl]-3-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:885732 HCAPLUS
DOCUMENT NUMBER: 136:11205
TITLE: Combinations of an endothelin receptor antagonist and an antiepileptic compound having analgesic activity
INVENTOR(S): Dooley, David James
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001091736	A2	20011206	WO 2001-US14793	20010508
WO 2001091736	A3	20021017		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1289558	A2	20030312	EP 2001-939002	20010508

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

BR 2001011207	A	20030401	BR 2001-11207	20010508
JP 2003535061	T2	20031125	JP 2001-587752	20010508
US 2003232787	A1	20031218	US 2002-296792	20021126

PRIORITY APPLN. INFO.: US 2000-208259P P 20000531
WO 2001-US14793 W 20010508

OTHER SOURCE(S): MARPAT 136:11205

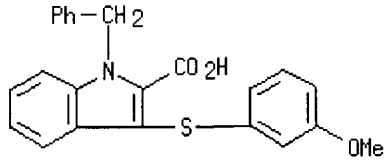
AB The present invention is a novel combination effective for alleviating pain comprising an endothelin receptor antagonist or a salt and from 1 to 3 compds. independently selected from the group consisting of antiepileptics having analgesic activity, and pharmaceutical compns. comprising the compds. The administration of endothelin receptor antagonists in these novel combinations results in an improved redn. in the frequency and severity of pain. The incidence of unwanted side effects can be reduced by these novel combinations in comparison to using higher doses of a single agent treatment to achieve a similar therapeutic effect. Thus, tablets contained 4-(7-ethyl-1,3-benzodioxol-5-yl)-2-[2-(trifluoromethyl)phenyl]-2H-1,2-dihydro-1,2-benzothiazine-3-carboxylic acid 1,1-dioxide potassium salt 25, gabapentin 25, lactose 50, corn starch (for mix) 10, corn starch (paste) 10, and Mg stearate 5 mg. The combinations of the present invention are effective at reversing static allodynia,and are thus useful for the treatment of pain.

IT **175339-72-7**

RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(combinations of endothelin receptor antagonist and antiepileptic having analgesic activity)

RN 175339-72-7 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 3-[(3-methoxyphenyl)thio]-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



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L8 ANSWER 7 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:661388 HCAPLUS
DOCUMENT NUMBER: 135:226878
TITLE: Synthesis of N-benzyl-indolyl(benzyloxy)amido

derivatives as PDE-IV inhibitors

INVENTOR(S): Labelle, Marc; Sturino, Claudio; Lachance, Nicolas; MacDonald, Dwight

PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.

SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001064639	A2	20010907	WO 2001-CA270	20010302
WO 2001064639	A3	20020228		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002068756	A1	20020606	US 2001-797083	20010301
US 6436965	B2	20020820		
EP 1263728	A2	20021211	EP 2001-913422	20010302
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003525273	T2	20030826	JP 2001-563482	20010302

PRIORITY APPLN. INFO.: US 2000-186571P P 20000302
WO 2001-CA270 W 20010302

OTHER SOURCE(S): MARPAT 135:226878

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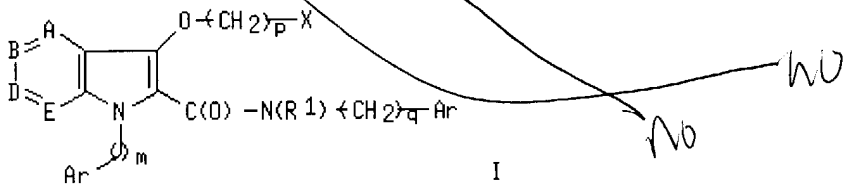

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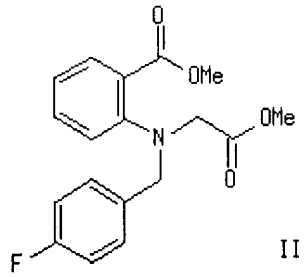

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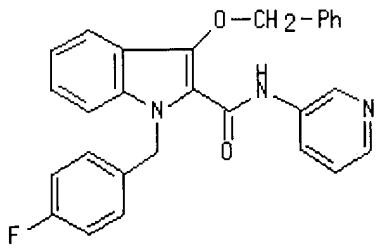


III

AB Title compds. I [A, B, D, E = N or CR2 and the others = CR2; q = 0 - 1; p, m = 0 - 2; R1 = H, (hydroxy)alkyl; R2 = H, halo, (halo)alkyl, hydroxyalkyl, CN, arom. or nonarom. ring system contg. 1 - 4 heteroatoms selected from O, S, N, alkoxy, oxyamide, etc.; X = cycloalkyl or Ar; Ar =

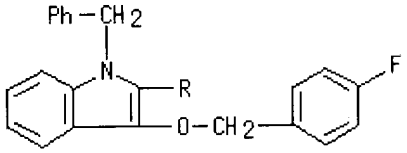
(un)substituted (Ph, thienyl, thiazolyl, pyridyl, oxazolyl, tetrazolyl, pyrimidinyl, pyrazinyl and pyridazinyl)]were prepd. Over 150 compds. were disclosed. For instance, Me 2-aminobenzoate was alkylated with 4-fluorobenzyl bromide (K2CO3, MEK, reflux, 8 h.). The resulting ester was sapond. (NaOH, MeOHaq reflux, 2 h.), N-alkylated with Me bromoacetate (K2CO3, MeOHaq, reflux, 18 h.) and treated with CH2N2 to afford II. Diester II was cyclized (NaOMe, MeOH, reflux, 30 min.), O-alkylated with benzyl bromide (K2CO3, MEK, reflux, 2 h.), sapond. (NaOH, EtOHaq, 90°C, 40 min.) and finally coupled to 3-aminopyridine (SOCl2, i-Pr2NEt, room temp., 3 h.) to yield III. I are PDE-IV inhibitors (no data) useful for treating, e.g., **inflammation**, muscle spasm, chronic bronchitis, etc.

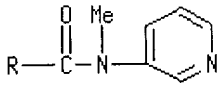
IT **359001-30-2P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; synthesis of N-benzyl-indolyl(benzyloxy)amido derivs. as PDE-IV inhibitors)

RN 359001-30-2 HCAPLUS

CN 1H-Indole-2-carboxamide, 3-[(4-fluorophenyl)methoxy]-N-methyl-1-(phenylmethyl)-N-3-pyridinyl- (9CI) (CA INDEX NAME)





L8 ANSWER 8 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:526057 HCAPLUS
DOCUMENT NUMBER: 135:107248
TITLE: Preparation of indole-2-carboxylic acids as MCP-1 receptor antagonists
INVENTOR(S): Faull, Alan Wellington; Kettle, Jason Grant
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001051466	A1	20010719	WO 2001-GB69	20010111

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

BR 2001007404	A	20021008	BR 2001-7404	20010111
EP 1252142	A1	20021030	EP 2001-900494	20010111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003519683	T2	20030624	JP 2001-551848	20010111
EE 200200394	A	20031215	EE 2002-394	20010111
BG 106894	A	20030430	BG 2002-106894	20020702
US 2003144339	A1	20030731	US 2002-169717	20020709
NO 2002003380	A	20020903	NO 2002-3380	20020712

PRIORITY APPLN. INFO.: GB 2000-626 A 20000113
WO 2001-GB69 W 20010111

OTHER SOURCE(S): MARPAT 135:107248

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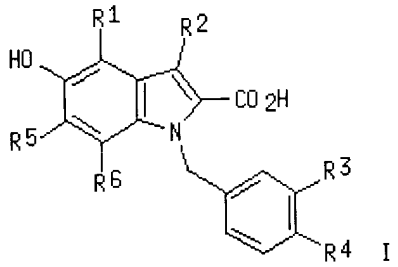
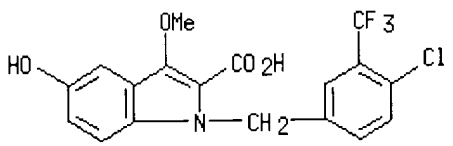


I

AB The title compds. [I; R1 = H, halo, OMe; R2 = H, halo, Me, Et, OMe; R3 = halo, CF3; R4 = halo, CF3; R5 = H, halo; R6 = H, halo; provided that when R5 and R6 are both H atom, and one of R3 or R4 is Cl or F, then the other is not Cl or F] and their prodrugs which have useful activity for the treatment of **inflammatory** disease, specifically in antagonizing an MCP-1 mediated effect in a warm-blooded animal such as a human being, were prepd. and formulated. Thus, reacting Et N-(3-trifluoromethyl 4-chlorobenzyl)-5-acetoxyindole-2-carboxylate (prepn. given) with NaOH in H2O/MeOH followed by treatment with 2M HCl afforded 71% I [R1, R2, R5, R6 = H; R3 = CF3; R4 = Cl]. The tested compds. I had IC50's of ≤ 50 μM in the hMCP-1 receptor binding assay.

IT **350596-52-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of indole-2-carboxylic acids as MCP-1 receptor antagonists)

RN 350596-52-0 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[[4-chloro-3-(trifluoromethyl)phenyl]methyl]-5-hydroxy-3-methoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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